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PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DO MOVIMENTO

INICIAÇÃO DO ANDAR E DOENÇA DE PARKINSON: INFLUÊNCIA DA PRESENÇA DE UM OBSTÁCULO, DA TAREFA COGNITIVA E DA INFORMAÇÃO SENSORIAL

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Iniciação do andar e doença de Parkinson: influência da presença de um obstáculo, da tarefa cognitiva e da informação sensorial

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Orientador: Prof. Dr. Fabio Augusto Barbieri

Tese apresentada ao Faculdade de Ciências do Câmpus de Bauru, Universidade Estadual Paulista, como parte dos requisitos para obtenção do título de Doutor em Ciências do Movimento.

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ATA DA DEFESA PÚBLICA DA TESE DE DOUTORADO DE LUCAS SIMIELI, DISCENTE DO PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DO MOVIMENTO, DA FACULDADE DE CIÊNCIAS - CÂMPUS DE BAURU.

Aos 17 dias do mês de agosto do ano de 2021, às 13:30 horas, por meio de Videoconferência, realizou-se a defesa de TESE DE DOUTORADO de LUCAS SIMIELI, intitulada **INICIAÇÃO DO ANDAR E DOENÇA DE PARKINSON: INFLUÊNCIA DA PRESENÇA DE UM OBSTÁCULO, DA TAREFA COGNITIVA E DA INFORMAÇÃO SENSORIAL**. A Comissão Examinadora foi constituida pelos seguintes membros: Prof. Dr. FABIO AUGUSTO BARBIERI (Orientador(a) - Participação Virtual) do(a) Departamento de Educação Física / UNESP - Faculdade de Ciências de Bauru - SP, Prof. Dr. RENATO DE MORAES (Participação Virtual) do(a) Programa de Pós-graduação em Educação Física e Esporte / Universidade de São Paulo - Escola de Educação Física e Esportes de Ribeirão Preto - SP, Prof. Dr. RODRIGO VITORIO (Participação Virtual) do(a) Docente credenciado no Programa de Ciências da Motricidade / Northumbria University – Reino Unido, Prof. Dr. LUIS AUGUSTO TEIXEIRA (Participação Virtual) do(a) Departamento de Biodinâmica do Movimento do Corpo Humano / Escola de Educação Física e Esporte - Universidade de São Paulo / SP, Profa. Dra. MARIA ELISA PIMENTEL PIEMONTE (Participação Virtual) do(a) Depto. de Fisioterapia/FM/USP/São Paulo. Após a exposição pelo doutorando e arguição pelos membros da Comissão Examinadora que participaram do ato, de forma presencial e/ou virtual, o discente recebeu o conceito final: **APROVADO**. Nada mais havendo, foi lavrada a presente ata, que após lida e aprovada, foi assinada pelo(a) Presidente(a) da Comissão Examinadora.

Prof. Dr. FABIO AUGUSTO BARBIERI

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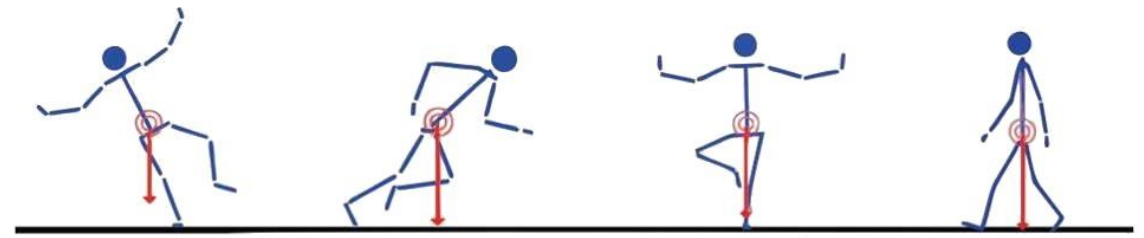

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Resumo

A dificuldade na iniciação da marcha é recorrente em pacientes com doença de Parkinson (DP). A ausência de ajustes posturais antecipatórios (APAs) que ocorrem antes do início do movimento de andar são as principais causas de dificuldades nesta população e está relacionada com os sinais e sintomas comuns na DP como acinesia e instabilidade postural. O aumento na complexidade motora e na demanda cognitiva e sensorial pode prejudicar ainda mais a iniciação do andar de pacientes com DP. Assim, este estudo tem como objetivo investigar o efeito da presença de obstáculo, da tarefa dupla e da restrição sensorial durante o início do andar em pacientes com DP. Para isso, uma sequência quatro estudos foram desenvolvidos. No primeiro estudo foi realizada uma revisão sistemática com objetivo de determinar as mudanças nos parâmetros de centro de pressão, APAs e espaço-temporais durante a iniciação da marcha de pacientes com DP. Os estudos posteriores tiveram como objetivo verificar o efeito da presença do obstáculo de diferentes alturas na iniciação do andar, de analisar a influência da carga cognitiva e de determinar a contribuição da informação visual e proprioceptiva na iniciação do andar com e sem a presença do obstáculo em pacientes com DP. Em cada estudo participarão entre 13 e 15 pacientes com DP e o mesmo número idosos neurologicamente sadios. Todos os participantes foram avaliados cognitivamente, sendo que os pacientes com DP ainda foram avaliados clinicamente. Os resultados da revisão sistemática ilustram a importância do estudo da iniciação do andar, uma vez que o grupo DP apresenta dificuldades em iniciar o primeiro passo, diminuindo o número de APA para realizar esse início de forma mais segura e eficiente. Ainda, revelou que pouco se sabe sobre a influência de tarefa duplas durante essa fase, sendo poucas as evidências, mas que já indicam a dificuldade ainda maior do grupo DP em lidar com duas ou mais tarefas durante essa etapa do andar. Nosso estudo sobre altura do obstáculo mostrou uma característica interessante sobre os APA: o grupo DP mantém os parâmetros dos APA praticamente inalterados, independente da altura. Os ajustes para iniciar a tarefa com obstáculo são, majoritariamente, nos ajustes espaço temporais (comprimento, largura, duração e velocidade do passo). Os dados dos estudos 3 e 4, somam aos achados do estudo 2, evidenciando a robustez dos dados dos APAs. Ou seja, indivíduos com DP conservam os APA durante o início do andar em ambientes mais complexos, modificando parâmetros espaço-temporais do andar. Ainda, quando a visão dos membros inferiores é bloqueada, os parâmetros espaço-temporais sofrem mais ajustes, corroborando com a literatura sobre a necessidade de informação visual maior para indivíduos com doença de Parkinson. Dessa forma, é possível afirmar que pessoas com DP apresentam dificuldades na iniciação do andar, de modo que os APA são menores e mais lentos quando comparados a idosos sem DP. Entretanto, esses parâmetros são pouco modificáveis, elucidando a robustez que o sistema carrega para modifica-los de acordo com a tarefa.

Abstract

Difficulty in gait initiation is recurrent in people with Parkinson's disease (PD). The absence of anticipatory postural adjustments (APAs) that occur before the beginning of walking is the main cause of difficulties in this population and is related to common signs and symptoms in PD, such as akinesia and postural instability. The increase in motor complexity and cognitive and sensory demand can further impair gait initiation in PD patients. Thus, this study aims to investigate the effect of the presence of obstacles, dual-task, and sensory restriction during the beginning of walking in people with PD. For this, a sequence of four studies was developed. In the first study, a systematic review was performed to determine changes in the center of pressure, APAs, and spatiotemporal parameters during gait initiation in PD patients. Further studies aimed to verify the effect of the presence of the obstacle of different heights on gait initiation, to analyze the influence of cognitive load, and to determine the contribution of visual and proprioceptive information in gait initiation with and without the presence of the obstacle in PD patients. Between 13 and 15 patients with PD and the same number of neurologically healthy elderly people participated in each study. All participants were cognitively evaluated, and patients with PD were clinically evaluated either. The results of the systematic review illustrate the importance of studying the initiation of walking, since the PD group has difficulties in performing the first step, reducing the number of APAs to perform this initiation more safely and efficiently compared to people without PD. Furthermore, it revealed that little is known about the influence of dual tasks during this phase, with little evidence, but that already indicates the even greater difficulty of the PD group in dealing with two or more tasks during this stage of walking. Our study on the height of the obstacle showed an interesting characteristic about the APA: the DP group maintains the parameters of the APA practically unchanged, regardless of the height. The adjustments to start the task with an obstacle are, mostly, in the spatiotemporal parameters (step length, width, duration, and velocity). Data from studies 3 and 4 add to the findings from study 2, showing the robustness of data from the APAs. In other words, individuals with PD changing APAs during only gait initiation in more complex environments, modifying the spatiotemporal parameters of gait in most of cases (easier tasks). Moreover, when the vision of the lower limbs is blocked, the spatiotemporal parameters were even more affected, demanding further adjustments. These results corroborate with the literature on the need for greater visual information for individuals with Parkinson's disease. Thus, it is possible to state that people with PD have difficulties in starting to walk so that the APAs are smaller and slower when compared to elderly people without PD. However, these parameters are dependent of task difficulty, elucidating the robustness that the system loads to modify them according to the task, doing all changes on spatiotemporal parameters to perform the task.

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Contextualization

Parkinson's disease (PD) has a significant world-wide prevalence (VAN DEN EEDEN et al., 2003), which has attracted the interest of researchers and governments in research aimed at diagnosis, prevention, treatment and care for patients with this disease. Neurodegeneration of dopaminergic neurons, mainly those of substantia nigra pars compacta, characterizes PD (TAKAKUSAKI et al., 2004). The dopaminergic decrease inhibits both motor systems, the thalamus-cortical and the brainstem, and compromises other brain areas (OBESO et al., 2000). As a result of this pathological condition, PD patients present some well-defined signals and symptoms, like rest tremor, postural instability, muscle rigidity, akinesia (difficulty to initiate movement). They also present bradykinesia (slowness of movements) and hypometry (decreased range of motion) (HUGHES et al., 2002). Among these signs and symptoms, we highlighted for this project akinesia, which seems to impair anticipatory postural adjustments (APA) in gait initiation (HALLIDAY et al., 1998). We also address postural instability, caused by motor and sensory deficits associated with PD, making it more difficult to use adequate strategies for safe gait initiation (COLNAT-COUBOIS et al., 2005).

Difficulty on gait initiation is observed in 16% of PD people (JANKOVIC et al., 1990). As consequence of akinesia and postural instability, PD people tend to be more careful and answer wrongly to an external perturbation compared to their matched-age healthy neurologically people (STOLZE et al., 2004; VITÓRIO et al., 2010; PIERUCCINI-FARIA et al., 2013). These symptoms respond only partially to dopaminergic drug which suggests that the effect of these symptoms could be the result of impair on the non-dopaminergic system, like locomotor region which includes pedunculopontine (PPN) and cuneiform nuclei (DEVAL et al., 2014). The greater and complex connections for PPN

are those mutual via with basal ganglia, mainly for globus pallidus internal. The PPN also has a substantial relation to the extrapyramidal area and reticular formation which has a significant role in generating the gait pattern, being the local where posture and gait are coordinated (TAKAKUSAKI et al., 2008). Due to PD, the link between basal ganglia, extrapyramidal area, and reticular formation seem to implicate in an impair release of the motor program, for example, the program of gait initiation (TAKAKUSAKI et al., 2008). Moreover, it has also been proposed that the difficulty in gait initiation occurs due to a dysfunction of basal ganglia (DELVAL et al., 2014). The inhibitory alterations on basal ganglia output and brainstem are necessary to initiate the movement and in the coupling of postural stability and locomotion. These physiological impairments help to explain the inappropriate PD patients behavior during gait initiation, generating troubles on anticipatory postural adjustments (APA) to initiate the gait and postural stability control.

Stereotyped preparation is necessary for APA to initiate the gait (HALLIDAY et al., 1998). The APA is a movement of the center of pressure (COP) before an evident foot movement (NOCERA et al., 2013). On gait initiation, the COP moves to posterior and lateral toward swing limb. Besides, there is an increase in ground reaction force toward support limb which is immobile (BRUNT et al., 2005). This change in body weight generates COP displacement backward and forward of swing limb, causing a postural instability. Then, the COP moves toward support limb and, after that, forward. Toe-off just occurs when COP moves forward (DELVAL et al., 2014).

PD people present limitations on APAs to correct COP adjustments and, consequently, initiate the gait (BRENIERE, 1986; DELVAL et al., 2014). PD people have a difficult to improve postural stability enough to adjust COP and initiate the gait (DELVAL et al., 2014). A feasible explanation is that PD people have low or no excitation on tibialis anterioris during APA in gait initiation (GANTCHEV et al., 1996).

As a consequence, the ground reaction forces in mediolateral and anteroposterior direction and COP changes, which characterizes APAs, becomes longer and weaker in PD people, increasing akinesia, with greater latency on APAs between the beginning of the movement and the first step (HALLYDAY, 2007; KRYSTKOWIAK et al., 2006; VAUGOYEAU et al., 2003). Gait initiation difficulty could be mainly related to episodes of freezing in PD people, who are, in a short period, unable to start the walk or continue moving forward (NUTT et al., 2011). Besides, these impairments on gait initiation are not only due to locomotor system deficits, vestibulocerebellar and/or sensory, but also due to inadequate activation of executive function (SIU et al., 2008), especially during the concomitant cognitive task (dual-task).

Dual-task situations interfere even more in gait initiation in PD people (YOGEV-SELIGMANN et al., 2012). Increased attention to external cues is an important factor to facilitate gait initiation, like stripes on the grounds or auditory cues, which could improve APAs (BURLEIGH-JACOBS et al., 1997). External cues help in the locomotor pattern in PD people (ROCHA et al., 2014; AZULAY et al., 1999; VITORIO et al., 2011), are capable of ameliorating psychomotor performance and decreasing the freezing episodes (GILADI et al., 1997). However, people, mainly with PD, have difficulty in maintaining their attention in these external cues when performing a concomitant task (dual task) with a motor task. This situation generates a competition for attentional sources, creating a task prioritization (YOGEV-SALIGGMAN et al., 2012).

Frequently, to perform a dual task, a prioritization will occur for that one which demands more stability (SHUMWAY-COOK et al., 1997; BLOEM et al., 2001; YOGEV-SELIGMANN et al., 2012; SIMIELI et al., 2015). This behavior occurs mainly in young adults and healthy older adults who can perform the parallel process by basal ganglia, being the putamen the “controller” of the tasks (ISODA et al., 2009;

REDGRAVE et al., 2010; YOGEV-SELIGMANN et al., 2012). It is the usual behavior, as in challenging situations as during gait initiation with a dual cognitive task (ISODA et al., 2009; REDGRAVE et al., 2010; YOGEV-SELIGMANN et al., 2012). However, in PD people this circuitry (putamen) is more prone to neurodegeneration than the associative circuitry of the striatum, which is responsible for goal-directed behavior (REDGRAVE et al., 2010). Due to this, PD people use more frequently the goal-directed behavior than usual behavior when performing a cognitive task with a motor task (REDGRAVE et al., 2010; YOGEV-SELIGMANN et al., 2012). This type of process to plan and execute a motor action is voluntary and has a rigid control and by serial processing, which needs a high cognitive demand, becoming slower and non-automatic (REDGRAVE et al., 2010; YOGEV-SELIGMANN et al., 2012). Therefore, the patient also prioritizes one task, mainly that one that leads to stability, but with a worse performance in a secondary task (cognitive).

Although, until now, only one study has investigated dual cognitive task effect on gait initiation in PD patients. Nocera and colleagues (2013) have studied the dual-task effect on gait initiation in healthy young adults, healthy older people and PD patients. All participants performed a cognitive task during gait initiation. The author found that dual-task did not change APAs on gait initiation for any group. However, during a dual cognitive task, PD patient increased the number of errors, indicating a task prioritization for a task that demands more stability. Despite these significant findings, questions related to more challenging tasks during gait initiation like obstacle avoidance are necessary, once this population shows impairments on motor circuitry, like showed previously. Obstacle avoidance increases, even more, the attentional prioritization for stability task, which could generate a deficit on integration between the attentional system and the movement start (YOGEV-SELIGMANN et al., 2012). Hence, the motor behavior could

be even more affected on gait initiation with obstacle avoidance, which is a common task during daily life (STOLZE et al., 2004; VITÓRIO et al., 2010).

Gait initiation with dual-task could be considered a dangerous task, especially for PD patients. Obstacle avoidance or circumvention is a challenge that increases the number of falls (LAJOIE et al., 2008; PAQUETTE and VALLIS, 2010), mainly in a PD patient whose falls are one-third during these tasks (STOLZE et al., 2004). Obstacle avoidance demands more from the individual, once three mechanisms need to be controlled. They are: i) action planning that determines how the motor planning will be used and the path to be walked (anticipatory control); ii) responses to expected perturbation which are related to APAs, resulting from segmented movements (predictive control); iii) unexpected responses which are adjustments arising from an unpredictable situation of the task, like an, unbalance or slip (reactive control) (MORAES and GOBBI, 2008; PATLA et al., 2003). Due to disease effects on locomotor circuitry (TAKAKUSAKI, 2008), PD patients are more compromised by obstacle during gait than their paired matched-controls (GALNA et al., 2010; VITÓRIO et al., 2010; STEGEMÖLLET et al., 2012). For gait initiation, the obstacle's presence on the first step could show a harmful effect for PD due to akinesia, and postural instability impairs APAs and gait initiation (DELVAL et al., 2013). However, there is only a little knowledge about obstacle avoidance during gait initiation, letting this one and other questions without conclusive answers.

Finally, we could not disregard that the effect of sensory integration deficits present in PD patients ((VAUGOYEAU et al., 2011; TAGLIABUE et al., 2009; VAUGOYEAU, 2014) could affect gait initiation. PD patients are more dependent on visual and proprioceptive information (ROCHA et al., 2014; VITÓRIO et al., 2011; ALMEIDA et al., 2005; AZULAY et al., 1999). However, this population shows

difficulties to select and use sensory information during gait (MORRIS et al., 1994a,b, 1996; VITÓRIO et al., 2014b). Furthermore, decrease, or absence of visual and proprioceptive information increases postural instability in these patients (JACOBS and HORAK, 2006), resulting in imbalances or falls. Other findings suggest that basal ganglia are involved in the sensory integration of visual and proprioception information when PD people need to walk toward a target in the darkness (ALMEIDA et al., 2005) or when they need to estimate obstacle height by foot elevation (MARDENS and ALMEIDA, 2012). However, the role of basal ganglia in sensory integration was recently discovered (ALMEIDA et al., 2005; KONCZAK et al., 2009), and there is a little information about the visual and proprioceptive contribution to gait initiation, which demands much sensorial information for proper execution, especially during obstacle presence.

Therefore, the present project aims to investigate the effect of an obstacle, dual task, and sensory integration during gait initiation. To achieve it, we developed a sequence of four studies. With the results of this current project, we hope that motor interventions can be upgraded and planned to improve gait initiation and mobility of PD patients. Moreover, some gaps in literature were filled in linked with disease pathogenesis (DJALDETTI et al., 2006), clarifying the main responsible for motor adjustments and sensory integration on gait, mainly on gait initiation, and helping to understand disease progression (MELAMED and POEWE, 2012).

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1 - Effect of Parkinson's disease on gait initiation: a systematic review

(Submitted to Parkinsonism and Related Disorders – Second round of review)

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Abstract

Gait initiation is often a problem for people with Parkinson's disease. Disorders of the basal ganglia, specifically affecting the dopaminergic neurons, lead to changes in muscle activation and motor output, causing changes in gait initiation in this population. This review aimed to assess the evidence on changes in gait initiation in people with PD and on factors influencing these changes. A literature search was conducted in 4 databases with the key words 'gait initiation', 'locomotion initiation' or 'walking initiation' with 'Parkinson' or 'Parkinson's disease'. We identified 88 potentially relevant manuscripts and maintained nine papers for analysis. Collectively these papers showed that gait

initiation in people with PD is compromised when compared to healthy controls. People with PD presented APAs with slower and smaller COP displacements and a smaller and slower first step compared to healthy older adults during gait initiation. These effects were aggravated by concurrent task performance and reduced by cueing but only partially reduced by medication (L-Dopa).

Keywords: gait initiation, anticipatory postural adjustments, Parkinson's disease.

INTRODUCTION

Gait initiation comprises all changes in posture and muscle activity that occur when people start to walk from a static standing position, which occur before the toe-off that initiates the first step[1]. This is a common motor task that requires an intricate muscle coordination, to generate a dissociation between the center of mass (COM) and center of pressure (COP)[2]. Gait initiation requires adequate anticipatory postural adjustments (APAs) to keep balance and move the COM forward[3] based on a proper integration of motor commands and sensory information [1], [3], [4]. APAs are generally assessed from COP movements that occur before apparent foot movement [2], [3]. The COP first moves posterior and lateral towards the swing limb, to accelerate the COM towards the stance limb[5], [6]. Subsequently, the COP will move towards stance limb and forward. Here we will refer to COP displacements, before toe-off, as APAs. Alterations in APAs during gait initiation may reflect impairments, which may expose individuals to balance loss and falls[7].

Patients with Parkinson's disease (PD) present motor and sensory impairments due to deficits of the basal ganglia[3], [7]. They are slower than their peers[7]–[9] and present joint rigidity[7], resting tremor[7], [8], postural instability and akinesia[3], [9], [10]. PD-related motor and sensory impairments seem to affect gait initiation. Recent findings suggest that PD alters APAs during gait initiation [1], [3], [4]. Cognitive demands may play a role in impaired gait initiation in PD patients, as the presence of a concurrent task aggravates these impairments [11]–[13]. Conversely cueing appears to facilitate gait initiation in PD patients [4].

It is important to understand how APAs and other spatial-temporal characteristics of gait initiation are affected by PD, as well as whether and how these effects are modified by factors like dual tasking, cueing and medication. Therefore, the present systematic

review aimed to assess evidence on changes in these aspects of gait initiation in people with PD and on factors influencing these changes.

METHODS

Search strategy and study selection

We searched the Cochrane Library, Scopus, PsycInfo and Pubmed databases for manuscripts on gait initiation in people with PD, published from January 1960 to May 2019. The search was performed by combining the terms 'gait initiation', 'locomotion initiation' or 'walking initiation' with 'Parkinson' or 'Parkinson's disease'. An additional search in the reference lists of retrieved papers and reviews within this field was performed to identify other possibly eligible manuscripts. This systematic review included only studies published in the English language that assessed gait initiation parameters in individuals with PD. Papers on animal models, robotics and/or without people without PD (i.e. young adults and/or older healthy subjects) were not included. In addition, for manuscripts presenting other groups besides PD patients, we only considered the PD group results. Methodological or descriptive studies, and papers without people with PD classification (Unified Parkinson Disease Rating Scale (UPDRS) or Hoehn and Yahr scale) were excluded.

Two independent reviewers (L.S. and L.F.I.I.) performed the literature search and assessment. Papers that did not describe gait initiation in PD were excluded based on the initial evaluation of titles and abstracts. Full texts were analyzed if the information presented in title and abstract was insufficient to decide about inclusion. In view of possible differences in terminology used by the researchers for relevant variables, we used a guideline with a list of synonyms to improve inter-reviewer reliability. The list of

synonyms included parameters related to gait, such as ‘step or stride length’, ‘step or stride width’, and ‘speed or velocity’.

Quality assessment

The quality of each study was defined as the ability to avoid bias and generate results that can be generalized. This definition includes the internal and external validity. Internal validity refers to whether results can be generalized to the population of interest. To assess the quality of the studies included in the present review, we used an assessment tool developed specifically for this type of systematic review[14] [15]. The tool consisted of 14 items, some of them with sub-items (Table 1). Each item/sub-item was rated between 0 and 1, where 1 was considered high quality, 0.5 was considered lacking information or clarity, and 0 was considered low quality. The scores for the 14 items were averaged to express the quality of each study. The quality assessment of each study included was performed by the two reviewers who performed the literature search. When there was discrepancy between reviewers, a third reviewer (F.A.B.) was consulted to solve the discrepancy. Manuscripts with an average score below 0.7 points were excluded from the present review.

Data extraction and analysis

The data on study source, such as: sample size, characteristics of participants (i.e. disease severity, cognitive characteristics and age of the participants), parameters of interest (i.e. APAs, COP and spatial-temporal parameters), task performed in the study (i.e. gait initiation with or without obstacle and sensory manipulation), outcomes and limitations of the study were extracted independently by the two authors who performed the literature search. The results of the papers were summarized descriptively using means, standard deviations, and minimum and maximum values.

RESULTS

The database search identified 88 potentially relevant manuscripts, from which the screening based on title and abstract identified nine studies assessing gait initiation (Figure 1). The full text screening identified nine studies on gait initiation in patients with PD, with or without a concurrent task, that were published between 2002 and 2020 (December). These nine studies were of high-quality (total average quality from 0.76 to 0.96) and were thus included in the present review (Table 1). The review thus comprised 167 patients with PD aged 64±3 years old, with Hoehn and Yahr scores from 1 to 3 and …. healthy controls. For those papers that reported UPDRS-III [2], [16]–[19], the average score in the patients was 28.8±9.7 points. A general description of each included study is given in Table 2. Five studies were conducted in Europe[3], [4], [16]–[18] and four studies in USA[1], [19]–[21]. Five studies included a concurrent task during gait initiation[1], [2], [4], [18]–[20]. Only one study did not present data on APAs[20], but did report kinematic parameters of gait initiation. Table 2 provides an overview of the main characteristics and findings of the included studies.

*********Figure 1********

PD effects on APAs and spatial-temporal parameters in gait initiation

Eight studies assessed APAs, and all showed that the APAs were altered in people with PD[1], [2], [4], [16]–[19], [21] (Table 2 and Figure 2). The results indicated slower COP movements and smaller COP displacements in patients with PD [1], [17], [19] [11]. Healthy matched controls presented a stereotypical COP movement during gait initiation[1], [2], [4], [18], [20], moving to the leading limb, and subsequently to the

trailing limb, people with PD presented delayed COP movement during gait initiation, with smaller and slower movements of the COP in both directions (anterior-posterior and mediolateral), coinciding with a longer delay between onset of the APAs and step initiation[1], [2], [18], [20].

People with PD reduced step velocity and step length during the first step [4], [16], [18], [19]. In addition, people with PD showed a longer delay between the onset of muscle activity and apparent foot movement compared to controls [1], [2], [4], [16]–[19], [21].

******* Table 1******

Concurrent task and sensory cueing and during gait initiation

Two studies[1], [18] assessed the effect of a concurrent task during gait initiation and two assessed effects of sensory cueing [19][4]. Regarding concurrent task performance, one study showed [1] that in people with PD, the concurrent task caused a smaller COP displacement in the mediolateral direction and a slower COP speed in mediolateral and anterior-posterior directions[1], compared healthy controls.

Regarding cueing, auditory cues influenced gait initiation both in people with PD and in neurologically healthy older individuals [18]. Attentional cues (e.g. a specific instruction given to the participants) improved gait initiation, acting like triggers. However, in cued gait initiation in patients with PD and freezing showed inappropriate APAs, defined as involving unnecessary movements prior to gait initiation, in 63% of trials and patients with PD without freezing showed inappropriate APAs in 51%, while healthy older adults did so in 48% of trials). McCandless and colleagues [4] assessed four types of cues during gait initiation (visual with a laser, auditory with a metronome, vibration metronome and

cane). They found that visual cues promoted increased COP displacements in both directions and decreased the number of freezing episodes in people with PD.

********** Figure2 **********

Medication effect

One study[19] investigated the effects of medication on gait initiation in patients with PD. The authors compared OFF-state (without medication) to ON-state and neurologically healthy older people. Patients with PD presented less pronounced medio-lateral COP displacements in the OFF-state. However, for other parameters analyzed, the authors did not find any difference between ON- and OFF-states[19]. The authors did not find significant differences between healthy subjects and subjects with PD in the size of the APAs during self-initiated steps,

******* Table 2 *********

DISCUSSION

This systematic review addressed the effects of PD on gait initiation, with a focus on APAs and spatial-temporal parameters of the first step. People with PD presented APAs with slower and smaller COP displacements and a smaller and slower first step compared to healthy older adults during gait initiation. These effects were aggravated by concurrent task performance and reduced by cueing but only partially reduced by medication (L-Dopa) during gait initiation. Possibly the deficits caused by PD in basal ganglia are responsible for the impairments on gait initiation in this population.

The slower and small first step in patients with PD might can be a result of the smaller and slower APA [1], [3] presented by this group. A reduction in COP

displacement in backwards direction decreases the forward acceleration of the COM [7], which limits the movement of the swing limb in the first step and reduces the generation of momentum to facilitate gait initiation [1]. This could be especially problematic when patients which can need to avoid an obstacle during gait initiation requiring a bigger than usual step.

The neurophysiology of PD may explain the slower gait initiation. The loss of dopaminergic neurons reduces the levels of dopamine, which impairs functioning of the basal ganglia [8]. This is reflected in an inability to initiate voluntary movements[22]. This inability may also be associated with alterations in supplementary motor and premotor areas[8], [23], which are thought to be important for generation of APAs [23]. Additionally, lesser activity of the premotor cortices, due to loss of dopaminergic neurons in substantia nigra, may disturb the motor programming required for precise gait control [8]. When facing a more complex environment, such as when having to perform a concurrent motor or cognitive task, other brain areas (e.g. temporoparietal cortex) may be involved in accurate gait initiation control[23]. Deficiencies in information processing could cause errors in APAs and freezing of gait [3], [23].

In addition, people with PD may have problems obtaining visual information [24], [25] possibly by loss of dopamine in retina[26] and compromised perception [27], and need more time to acquire precise visual information necessary for motor control [28], [29]. For safe and stable gait initiation, it's important to acquire correct information about foot placement locations [3], [30] and other environmental aspects (e.g. people crossing the planned path, obstacles, holes, etc.). Visual cues are a good strategy to improve the visual information acquisition, and consequently, gait initiation in people with PD, since other studies have focused the augment on motor output from the augment in sensorial

input (visual information, in this case). However, until now, there are no studies that have tried to understand the visual behavior in people with PD during gait initiation.

Visual cues apparently reduce the effects of basal ganglia malfunction, improving gait initiation in people with PD. Basal ganglia malfunction is thought to decrease supplementary motor area activity, leading to problems in preparation of movements[31]. In this perspective cues may be understood as "super-stimulation", leading to enhanced supplementary motor area activation through increased sensory input [32], leading to larger COP displacements in both directions and a the number of freezing episodes in people with PD.

Performing a concurrent task during gait initiation reduced and slowed COP displacement. Generally, PD patients appear to have a limited capacity to deal with more than one task simultaneously [11], [13], [33]. The divided attention often occurs when people with PD need to deal with internal attention control (directed relate to the main task – like walking) [34] plus another external factor, such as an obstacle, dual-task. The mechanism underlying dual task interference is still unclear. Initially, it has been described as a attentional resource competition[35]. Since in PD brain capacity is impaired, limited resources must be re-distributed between the tasks (e.g. gait initiation and dual-task)[36]. Another possible mechanism is the bottleneck model, postulating that tasks must be carried out sequentially (not in parallel), so, execution of one task needs to be prioritized at the cost of delaying the other (mostly, individuals prioritize the postural task, "posture-first" strategy[11]). However, the results reviewed suggest that the motor task (gait initiation) suffers from concurrent task performance and hence is not prioritized by PD patients.

The effect of dopaminergic medication on gait initiation unclear. Only a single study investigated the effects of dopaminergic medication on gait initiation in people with PD, and the effects of medication on gait initiation were limited (larger medio-lateral COP displacements in the ON-state[19]). Previous studies that investigated dopaminergic medication effects on gait in people with PD have reported increased gait velocity, step/stride length and decreased double support time in the ON-state compared to and the OFF-state[37]. However, this was not found during gait initiation [19]. One possible explanation is that the medication could not alter a robust parameter like APAs. Others studies have also shown that a "simple" task is not influenced by dopaminergic drug [38], [39]. So, gait initiation itself isn't a task that demand could be not high enough to be drug-dependent. So, it's important that future studies compare gait initiation between ON- and OFF- states and vary task complexity to verify the hypothesis that medication effect depend on task complexity.

In conclusion, gait initiation in people with PD is compromised compared to healthy controls. People with PD presented slower and smaller COP displacements and a smaller and slower first step during gait initiation. Cueing facilitates gait initiation in patients with PD, but auditory cues may increase the number of inappropriate APAs. Moreover, more evidence is needed to reach a conclusion on the effects of dopaminergic drug on gait initiation.

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Figure 1. Flowchart of manuscripts included for review.

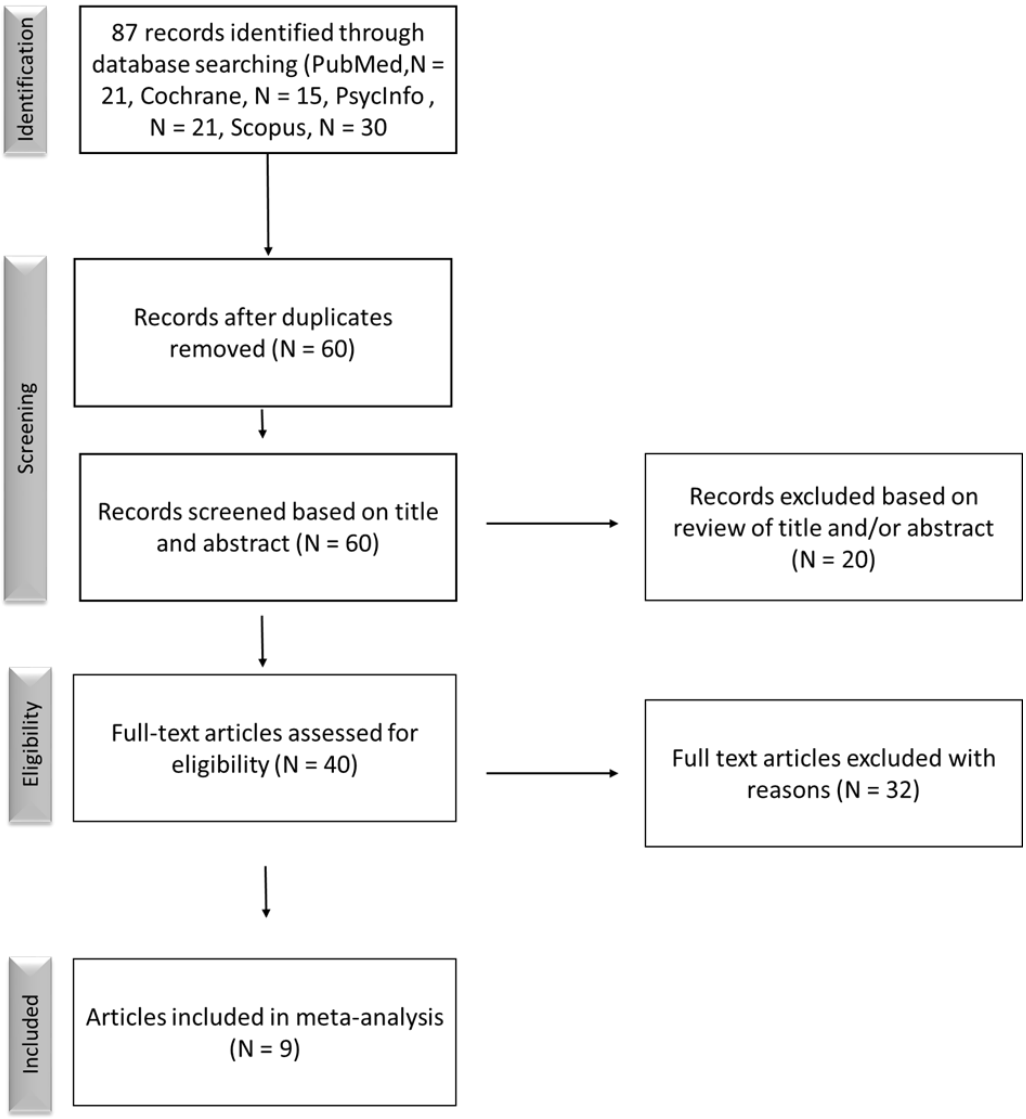


Table 1. Methodological quality appraisal results.

Question	Criteria	Marlin 2002[15]	Rocchi 2006[12]	Mancini 2009[11]	Vallbhajosula 2013[14]	Nocera 2013[1]	Tard 2014[13]	Delval 2014[2]	McCandless 2016[8]	Schlenstedt 2017[16]
1. Research aims or questions stated clearly	1 - Y; 0.5 - YL; 0 - N	1	1	1	1	1	1	1	0.5	1
	Control group	1	1	1	0.5	1	1	0	0	1
2. Participants detailed	PD group	1	1	1	1	1	1	1	1	1
	Number	1	1	1	1	1	1	1	1	1
	Age	1	1	1	1	1	1	1	1	1
	Sex	1	1	0	0	1	1	1	1	1
	Height	1	1	0	1	0	1	1	0	0
3. Recruitment and sampling methods described	1 - Y; 0.5 - YL; 0 - N	1	1	1	1	1	1	1	1	1
4. Inclusion and exclusion criteria detailed	1 - Y; 0.5 - YL; 0 - N	1	1	1	1	1	1	1	1	0.5
5. Controlled covariates	Height	1	1	1	1	0	1	1	0	0
	Age	1	1	1	1	1	1	1	0	0
	Sex	0	1	1	0	1	1	1	0	0
	Body mass	0	0	1	1	0	1	1	0	1
	UPDRS	1	1	1	1	1	1	1	1	1
	Sub total	0.6	0.8	1	0.8	0.6	1	1	0.2	0.5
6. Key outcome variables clearly described	1 - Y; 0.5 - YL; 0 - N	1	1	0.5	1	1	1	1	1	1
7. Adequate methodology able to repeat study	Participant sampling	1	1	1	1	1	1	1	0.5	1
	Equipment	1	1	1	1	1	1	1	1	1
	Procedure	1	1	1	1	1	1	0.5	1	1
	Data analysis	1	1	1	1	1	1	1	1	1

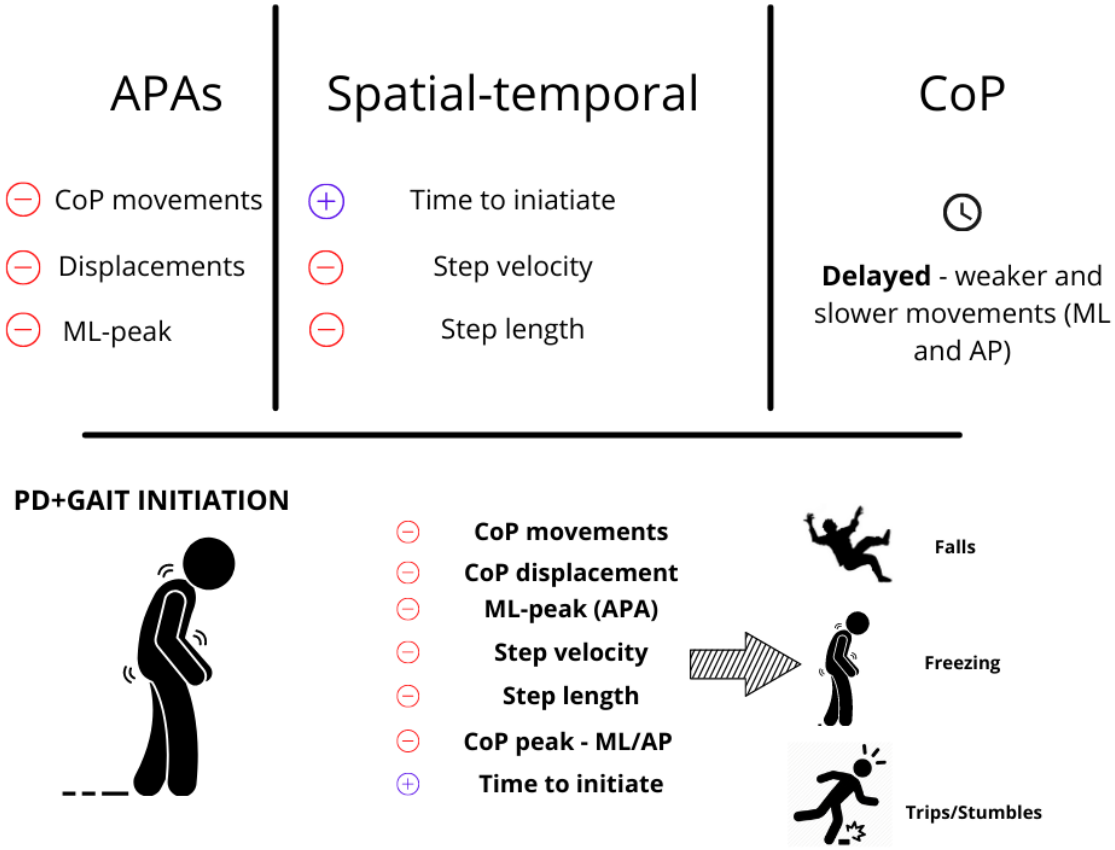
	Statistical analysis	1	1	0.5	1	1	1	1	1	0.5
	Sub total	1	1	0.9	1	1	1	0.9	0.9	0.9
8. Methodology able to answer research question	Equipment	1	1	1	1	1	1	0.5	1	1
	Procedures	1	1	1	0.5	1	1	1	1	1
	Data processing	1	1	0.5	1	1	1	1	0.5	1
	Statistical analysis	1	1	1	1	1	1	1	1	1
	Sub total	1	1	0.875	0.875	1	1	0.875	0.875	1
9. Reliability of the methodology stated	1 - Y; 0.5 - YL; 0 - N	1	1	0.5	1	1	0.5	1	0.5	1
10. Internal validity of the methodology stated	1 - Y; 0.5 - YL; 0 - N	1	1	1	0.5	1	1	1	1	1
11. Research question answered adequately in the discussion	1 - Y; 0.5 - YL; 0 - N	0.5	1	1	1	1	1	1	1	1
12. Key findings supported by the results	1 - Y; 0.5 - YL; 0 - N	1	1	1	1	0.5	1	0.5	1	1
13. Key findings interpreted in a logical manner which is supported by references	1 - Y; 0.5 - YL; 0 - N	1	1	1	1	0.5	1	1	1	0.5
14. Clinical implications stated	1 - Y; 0.5 - YL; 0 - N	1	1	0.5	1	1	1	1	0.5	0.9
	Total	**0.91**	**0.96**	**0.85**	**0.89**	**0.86**	**0.98**	**0.91**	**0.76**	**0.81**

Table 2. General characteristics of included studies. Gait initiation – GI; FOG – freezing of gait; PD – people with Parkinson's disease; APAs – Antecipatory postural adjusments; COM – center of mass; COP – center of pressure; UPDRS-III – Unified Parkinson's disease rating scale – motor section

Author	Aim(s)	Participants	Evaluation protocol	Parameters analyzed	Concurrent task
Martin et al., 2002[15]	To study differences in postural stability during GI between participants with PD (stages 1–3 of Hoehn and Yahr as) and older and younger adults.	3 groups of participants: subjects with PD, 69 years (SD 5, range 59–78); older subjects without PD, 69 years (SD 3, range 65–79); and younger subjects without PD, 27 (SD 3, range 22–35).	A 3-dimensional motion analysis system was used with 2 force platforms The participants initiated forward locomotion at a self-selected pace after receiving a verbal cue from one of the investigators.	Clinical: Hoehn and Yahr test. Force plate: data about COM and COP. Lateral displacement, difference between COP and COM position.	NO
Rocchi et al., 2006[12]	To study how the size of preparatory postural adjustments prior to GI, and step length and velocity depend on initial stance width in patients with PD (ON and OFF states) and in healthy older subjects.	21 subjects with idiopathic PD (16 males, 5 females, age 61.7±7.8 years, disease duration 16.2±9.2 years), and 24 age-matched healthy control subjects (18 males, 6 females, age 62.4±7.4 years).	Two steps starting with feet on a two-plate force-platform, from either narrow or wide stance width. They were instructed to voluntarily take two steps, starting with the right foot, at their normal, comfortable pace.	Clinical: Hoehn and Yahr Peak of COP at anterior-posterior direction and mediolateral direction, total elapsed time.	NO
Mancini et al., 2009[11]	To determine whether body-worn accelerometers could be used to characterize GI deficits in subjects with early-to-moderate, untreated PD.	11 patients with idiopathic PD and 12 age-matched healthy control subjects.	The subjects stood on a force plate at their comfortable stance but with hell-to-hell distance fixed at 10 cm. They were instructed to self-initiate two steps, starting with right foot, at their normal, comfortable pace.	Clinical: UPDRS III and the Hoehn and Yahr Scale. APAs parameters (time, peak, etc) from COP displacements and from L5 acceleration.	NO
Vallabhajosula et al., 2013[14]	To determine how multi-directional GI kinematics are affected by aging and PD.	11 PD (mean SD: 60.±2. years; disease duration: 11±3 years), 11 age- and gender matched older adults (60±2 years) and 12 healthy young adults (27±2 years).	Initial positioning of the feet and the stepping leg were self-selected. Upon hearing a verbal signal, the participants initiated gait toward the target. Each subject took a minimum of six steps prior to reaching the target.	Kinematics: step length, stance width, step velocity, step time, time to heel-rise and toe-off for both the legs. Angles: head, shoulder and pelvic segment angles	YES
Nocera et al., 2013[1]	To investigate the effect of a concurrent cognitive task on GI in three groups: patients with PD, healthy older and young adults.	13 patients with PD (aged 65±2 years), 13 healthy older adults (aged 66±2 years), 11 healthy young adults (20±2 years).	The data collection consisted of three single-task GI trials, three 0-back GI trials, and three 2-back GI trials.	Kinects: displacement and velocity of COP to determine APAs.	YES

Tard et al., 2014[13]	To establish whether or not a change in modulates APAs differently in patients with vs. without freezing of gait attentional load during GI.	30 patients with PD classified as patients with FOG (PD-FOGþ, n = 15) or without FOG (PD-FOG, n = 15) and 15 age-matched healthy controls.	The subjects had to press a button when they heard the target sound and start gait: 100 randomized stimuli: a low-pitched sound (standard: 1000 Hz, 40 ms, 80 dB and a probability of 0.85) or a high-pitched sound (target: 2000 Hz, 40 ms, 80 dB and a probability of 0.15) with an inter-stimulus interval of 5 s.	Kinects: displacement and velocity of COP to determine APAs.	YES
Delval et., 2014[2]	To establish whether auditory cueing improves the preparation and/or execution of GI in PD patients with a history of FOG.	30 PD patients with confirmed FOG under two randomised conditions: self-triggered (ST) gait and gait cued by a sound beep in off- and on-dopa conditions. APAs were evaluated.	Subjects were told to stand on the first force plate in the most natural, upright posture possible, with the two feet placed comfortably side by side. The externally triggered condition consisted in the subjects taking a step forward (and continuing to walk onwards) as soon as possible after hearing the signal.	APAs parameters (duration, direction, ect) were measured. For GI analysis, the spatial and temporal kinematic measurements were first-step speed, length (i.e., distance) and duration.	YES
McCandless et al., 2016[8]	To investigate the effects of three different types of cueing device in people with PD who experience freezing.	20 participants with PD (14 males, 68 years -range 49–84 years- and 11.5 years - range 1–23 years - since diagnosis.	Participants were asked to rise from a chair, stand briefly with one foot on each force plate, and then begin walking in their own time. This was to ensure that the instructions themselves did not act as a cue.	Parameters analyzed: percentage of freezing episodes, first and second step length, forward and sideways COM velocity, number of forward/backward sways and the number of sideways sways, forward and side to side COP velocity.	NO
Schlenstedt et al., 2017[16]	To characterize APAs across a variety of GI tasks in people with PD and healthy subjects	12 healthy subjects and 19 subjects with PD.	Subjects with PD were assessed during the off and on state. Three conditions were assessed: self-initiated, cued, and compensatory stepping.	The size of APA prior to stepping was assessed by analyzing the COP excursion during GI.	YES

Figure 2. Summary of gait initiation changes in patients with PD. ML = medio-lateral; AP – anterior-posterior



2 - Presence of an obstacle during gait initiation does not affect anticipatory postural adjustments but does affect spatial-temporal parameters in people with Parkinson's disease

(Submitted to Gait and Posture – First round of review)

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Abstract

Background: Presence of an obstacle could make gait initiation for patients with Parkinson's disease (PD) even difficult. However, especially low obstacles could work as a visual cue, known to facilitate gait in people with PD.
Research question: Analyze the effect of obstacle avoidance in the first step after gait initiation on APAs and spatial-temporal parameters of the first steps, and investigate the effects of different obstacle-heights on APAs and spatial-temporal parameters of gait initiation.
Methods: Thirty older people (15 PD group and 15 control group) participated in the study. All trials were performed in randomized order (5 trial each): gait initiation without obstacle, gait initiation with a low obstacle (3cm), gait initiation with an intermediate obstacle (15cm) and gait initiation with a high obstacle (25cm). Spatial-temporal gait parameters were collected with a Vicon Motion System® (200Hz). We calculated the length, width, duration, double support time and velocity of the two first steps. For APAs, a force plate (Accugait Forceplate AMTI® - 200Hz) was positioned in the start position. We first statistically compared groups across the conditions without and with an intermediate obstacle. Next, we statistically compared groups across the three obstacle conditions.
Results: No main effects of PD and obstacle presence on APAs were found. Main effects of PD showed that patients stepped slower, shorter and wider. Obstacle effects included greater first step length and duration. For the second step, with obstacle, step widths were smaller. Interaction effects showed that in the obstacle condition, people with PD presented longer second step duration and lower velocity than the control group and without obstacle. Second step widths were smaller for intermediate and low obstacles than for the high obstacle and step duration was shorter for low than the intermediate and high obstacles. An interaction indicated that at the high and intermediate obstacles, people with PD presented larger step widths on the first step than the control group. Overall, spatial-temporal parameters indicated that people with PD adopted a more conservative behavior than healthy controls. Furthermore, our results may suggest that, in PD patients, in stepping over a low obstacle, visual cueing offsets the mechanical challenge imposed, causing unimpaired stepping, initial steps over a high obstacle were more impaired in PD patients.
Significance: Our result highlights the robustness of gait initiation, once APA are not so easily malleable for motor control system. This is an innovative finding, once obstacle in gait initiation could be a strategy for training those people, teaching them to adjust themselves in order to avoid falls, especially in low ones.

Introduction (473 words)

Gait impairments are among the cardinal signs of Parkinson's Disease (PD)[1,2] and the necessity to deal with obstacles during ongoing gait may aggravate such impairments[3–5]. Obstacle avoidance is the third cause of falls among people with PD[6].

Previous studies have shown that obstacles of varying height may affect gait differently[4,7]. For example, Simieli and collaborators[4] showed that in the approach phase, gait adjustments were made earlier (three or four steps before the obstacle) for higher obstacles compared to lower obstacles in both PD patients and neurologically healthy individuals. In the crossing phase, no differences in step length and step speed were found between obstacle heights in neurologically healthy adults[8], while people with PD increased the variability of these parameters with obstacle height[9]. These effects of obstacle avoidance on gait in people with PD may also happen during gait initiation.

Gait initiation is a problematic task and can trigger freezing in people with PD[1]. During gait initiation, people with PD perform less pronounced anticipatory postural adjustments (APAs), with less or no activation of the tibialis anterior muscle, and perform shorter first steps compared to their neurologically healthy peers[1,10]. Considering these impairments, to avoid an obstacle during gait initiation can challenge the task in people with PD.

How obstacles affect gait initiation in people with PD is still unclear. Obstacle avoidance during the first step after gait initiation could be more challenging in PD due to increased demands on motor output and visual-spatial integration. This would be expected especially for higher obstacles, requiring more of the motor circuitry and attention[11,12]. On the other hand, a low obstacle in the first step could be considered a visual cue, which could help people with PD, similar to the effect of cues on the ground in ongoing locomotion[13,14]. The increased sensory input may facilitate motor output through the visuo-cerebellar pathway[15,16],

and facilitate gait initiation. Therefore, the presence of an obstacle in the first step could either impair or facilitate gait initiation in PD patients and this is likely obstacle-height dependent.

The purpose of the present study is to i) analyze the effect of obstacle avoidance in the first and second steps after gait initiation on APAs and step spatial-temporal parameters, and ii) investigate the effects of obstacle-height (3cm, 15cm and 25cm) on APAs and step spatial-temporal parameters of gait initiation in people with PD and neurologically healthy individuals. Considering the above, our hypotheses are: i) people with PD would show impaired gait initiation (greater APAs, smaller step length and higher step duration) compared to controls, ii) those impairments would be observable for higher obstacles (15cm and 25cm) but not for a lower obstacle (3cm) – they would decrease step length and increase step width for higher obstacle. On the other hand, the lower obstacle would help for APAs (decreasing it), increasing step length or keep it unaltered.

Methods (684 words)

2.1) Participants

Fifteen people with PD (PD group) and 15 matched neurologically healthy people (control group) participated in this study (Table 1). The number of participants was based on a power analysis using an alfa level of 0.05 and a power of 95% and data on APAs from Delval and colleagues[10] (G-power) – the analysis indicated a minimum number of thirteen people in each group. The following exclusion criteria were considered for the sample composition: aged below 50 years, Hoehn & Yahr scale above stage III (H&Y), history of orthopedic problems, and vision problem that could impossibilities the experimental protocol. Moreover, as an inclusion criterion, the individuals with PD were required to be currently receiving dopaminergic medication. Finally, both groups were evaluated with the Mini-Mental Status Exam – MMSE (the score was adjusted according to years of schooling[17]). A score below 24

points was considered an exclusion criterion. Only for PD group, subjects were evaluated through Unified Parkinson's Disease Rating Scale (UPDRS) (see Table 1).

2.2) Experimental design

The study was approved by Ethical local committee (CAAE 64921917.9.0000.5398) and the participants gave their consent to participate in the study. Clinical (Hoehn & Yahr, UPDRS and MMSE) and gait initiation evaluation were conducted in "ON state" phase of dopaminergic medication (approximately one hour after medication intake) for PD group.

All trials were performed in randomized order and each participant performed five trials in the following conditions: unobstructed gait initiation, and gait initiation with a low obstacle (3cm), an intermediate obstacle (15cm) and a high obstacle (25cm) in the first step. Before starting the trial, the participant was asked to close the eyes to avoid a priori planning according to the condition. Only after the command to start the trial ("Go"), the participant opened the eyes and performed the task. The evaluator reinforced the importance to keep the eyes closed until after the Go command. If the participant did open the eyes, the trial was excluded and performed again. For obstacle avoidance conditions (Figure 1), the obstacle was positioned at 10% of the participant's height in front of the starting position. We've chosen to standard the distance of 10% of participant's height in order to prevent more difficult from those shorter, and it would be needed an "artificial" adaptation if we didn't. Participants were instructed to avoid contact with the obstacle.

*****Figure 1 near here*****

2.3) Data collection

Spatial-temporal gait parameters were collected by a Vicon Motion System® with 8 cameras (Bonita System Cameras) sampling at a frequency of 200 Hz. For calculating these

parameters, we used 39 reflected markers that were positioned according to the Full Body Plug-in-gait protocol (Vicon Motion System®). We calculated the length, width, duration, double support time (percentage of step duration) and velocity of the two first steps (steps 1 and 2 in the Figure 1). Moreover, we've calculated variables related to the obstacle, toe-clearance and horizontal obstacle-foot distance[7,18–20]. For APAs, a force plate (Accugait Force plate AMTI®) sampling at 200 Hz was positioned in the start position (Figure 1). APAs were determined as any adjustments/alteration in center of pressure (CoP) that occurred before apparent foot movement, based on displacement and velocity of the heel marker[21]. APAs started with the initial movement of the CoP and ended when the CoP was in the most posterior and lateral in direction towards the stance leg. Anterior-posterior (AP) and medial-lateral (ML) displacement, amplitude and mean velocity were calculated for CoP position during gait initiation.

2.4) Statistical analysis

The significance level was set at 0.05. For participant characteristics, unpaired sample Student t-tests were employed to compare PD group and control group. The spatial-temporal and APA parameters were compared according to our questions i) effects of obstacle avoidance during gait initiation: two-way ANOVAs, with group as a between-subjects factor (PD group vs control group) and condition (no obstacle vs intermediate obstacle) as a within-subjects factor. For this analysis, we used the intermediate obstacle as it is used as curb height according to the Brazilian Association of Technical Norms[7,20]; ii) effects of obstacle-height on gait initiation: two-way ANOVAs, with group as a between-subjects factor (PD group vs control group) and condition as within-subjects factor (low obstacle vs intermediate obstacle vs high obstacle). Tukey post hoc tests were carried out to identify the significant differences when indicated by interaction effects.

Results (737 words)

For participant characteristics, t-tests did not reveal significant differences between groups in any of the parameters analyzed (Table 1). For obstacle conditions, we've registered 6 obstacle's touches for PD group (3 participants) and 2 obstacle's touches for control group (1 participant). All trial with obstacle touches were performed again and discarded from analysis.

*****Table 1 near here*****

3.1) *Effects of PD and obstacles on gait initiation*

APA parameters

There were no group effects on APA parameters in any of the conditions analyzed ($F_{1,28}$=3.748, p>0.05), neither it was not found there a main effect of the presence of the obstacle (intermediate) ($F_{6,23}$=1.020, p=0.437). Also, there was no effect of interaction group*obstacle ($F_{6,23}$=1.578, p=0.199)

Spatial-temporal parameters

For spatial-temporal parameters, a main effect of group was found in step-1 and step-2 on step width ($F_{1,28}$=8.844, p<0.006), step duration ($F_{1,28}$ =11.673, p<0.001), and step velocity ($F_{1,28}$ =16.965, p<0.001) and, in step-2 on the double support time ($F_{1,28}$=34.128, p<0.001). PD group presented higher values than controls for step width, duration of steps and double support phase than healthy participants. For step velocity on both steps, the PD participants presented lower values compared to the controls (both p<0.001).

Main effects of obstacle were found on step-1 length ($F_{1,28}$ =45.985, p<0.001), duration ($F_{1,28}$= 6.442,p<0.001), double support phase ($F_{1,28}$=19.788, p<0.001), velocity ($F_{1,28}$=18.034,

$p<0.001$), and on step-2 width ($F_{1,28}=77.615$, $p<0.001$) and double support phase ($F_{1,28}=70.261$, $p<0.001$). With obstacle, both groups presented greater step-1 length ($p<0.001$), longer step-1 duration ($p<0.001$) and shorter step-1 double support phase ($p<0.001$) compared to unobstructed gait initiation. For step-2, with obstacle, step widths were smaller ($p<0.001$) and double support phase ($p<0.001$) were shorter compared to without obstacle.

Group*condition interactions were found for step-2 duration ($F_{1,28}=10.338$, $p<0.003$) and step-2 velocity ($F_{1,28}=130.015$, $p<0.001$). In the obstacle condition, PD group presented longer step-2 duration ($p<0.001$) and slower step-2 velocity than the control group. The groups presented contrary adjustment during gait initiation with obstacle avoidance compared to unobstructed gait initiation: the control group had shorter step-2 duration ($p<0.001$), while PD group had longer step-2 duration ($p<0.001$) with obstacle.

3.2) Effects of obstacle-height on gait initiation

APA parameters

A main effect of obstacle height was found for AP-displacement ($F_{2,56}=3.635$, $p<0.03$). The post-hoc test indicated higher values of AP-displacement for the high obstacle than the intermediate obstacle ($p<0.04$). Moreover, a group effect was indicated ($F_{6,23}=2.705$, $p<0.03$), with higher values for ML-displacement in PD group ($p<0.03$). No group*condition interactions were found ($F_{2,56}=1.068$, $p=0.345$).

******Figure 2 near here******

3.3) Spatial-temporal parameters

ANOVA indicated lower values of step-1 length ($p<0.01$), step-1 ($p<0.001$) and step-2 ($p<0.001$) velocity for PD group compared to control group. Also, PD group had greater values

for step-2 width (p<0,001), step-1 (p<0.002) and step-2 duration (p<0.001) and double-support phase step-2 (p<0.001) compared to control group (Figure 3).

*****Figure 3 near here*****

Main effects of obstacle height were found on step-1 length ($F_{2,56}$=4.477, p<0.01), width ($F_{2,56}$=19.747, p<0.001), duration ($F_{2,56}$=33.678, p<0.001) and velocity ($F_{2,56}$=7.598, p<0.001), and on step-2 width ($F_{2,56}$=13.771, p<0.001), duration ($F_{2,56}$=5.599, p<0.006) and velocity ($F_{2,56}$=24.594, p<0.001 – Table 2). For step-1, the high obstacle condition increased the step length compared to the intermediate obstacle (p<0.04) and it increased the step width compared to the low obstacle (p<0.001). Step-2 widths were smaller for intermediate and low obstacles than for the high obstacle (p<0.001) and step duration was longer for high and intermediate obstacles compared to the low obstacle (p<0.04 and p<0.04, respectively).

A group*obstacle interaction was found for step-1 width ($F_{2,56}$=4.554, p<0.01). For step-1 width, at the high and intermediate obstacles, PD group presented higher values than the control group (p<0.001 and p<0.027, respectively).

*****Table 2 near here*****

3.4) *Obstacle clearance*

ANOVA indicated main effects of group ($F_{4,25}$ = 5.984, p <0.001) and condition ($F_{2,56}$ = 19,700, p <0.001) as well as group*condition interactions ($F_{8,106}$ = 2,854, p <0.009). PD group presented shorter horizontal obstacle-foot distances and toe clearance (both p<0.001) for the trailing limb, and larger horizontal obstacle-foot distance (p<0.01) for the leading limb than the controls. For the high obstacle, larger horizontal obstacle-foot distances of the trailing limb

($p<0.005$) and lower toe clearance of the leading limb ($p<0.001$) were found in comparison with other conditions.

A group*condition interaction was found only for horizontal obstacle-foot distance of the leading limb ($F_{2,56} = 10.662$, $p<0.001$). The control group presented greater values compared to the PD group in all obstacle conditions ($p<0.001$). Moreover, only for the PD group, the horizontal obstacle-foot distance in the condition with high obstacle was greater compared to other conditions ($p<0.001$).

Discussion (1073 words)

The aim of the study was to determine whether people with PD and neurological healthy people change gait initiation due to the presence of an obstacle and whether obstacles of different height affect differentially gait initiation. To our knowledge, this is the first study to demonstrate that i) both people with PD and neurological healthy people changed spatial and temporal parameters during gait initiation with obstacle avoidance rather than change the APAs; our results indicated that APAs were not affected by obstacle presence, and ii) the obstacle height affected spatial-temporal parameters of the first step after gait initiation: while obstacles greater than 15 cm were more challenging for people with PD, requiring larger base of support and increased horizontal obstacle-foot distance of leading limb, low obstacle (5 cm) was dealt without any adjustment of APAs and spatial-temporal parameters.

4.1) Presence of obstacle during gait initiation

The presence of an obstacle during gait initiation affected spatial and temporal parameters of the first and second step but not APAs. The obstacle presence (15 cm) appeared no imposing a big challenge for either of the groups, enabling that only adjustments on steps spatial and temporal parameter were enough to initiate safely the gait and avoid the obstacle.

Such obstacle heights are commonly present as curbs and stairs in Brazil, in accordance with standards of the Brazilian Association of Technical Norms (ABNT)[7,9], and participants should be relatively easy to deal with obstacles of this height, according previous studies found[18,20,22]. APAs are related to the body movement preparation before the start of walking[1,23] and involve all forces acting in the body (muscle forces and gravity). Considering that people with PD have loss of dopamine decreasing muscle activation[1,21] and, consequently, impairing APAs, we can suggest that APAs seemed to be robust parameter for gait initiation. However, people with PD adopted a more conservative behavior – greater step width, step duration, and double support phase – in the presence of obstacle during gait initiation, which supports the notion that this group prioritizes safety during motor tasks[24,25]. Once neurological pathways are damaged by loss of dopamine, motor control becomes less precise, which should be compensated to avoid falls.

APAs are not so easily changeable. Despite we need to adjust ourselves before an action, it is important to notice that APAs keep the same behavior until obstacles with 15cm height. Even in PD people, in which the dopaminergic system is impaired and the motor adjustments are compromised[26], APAs were not changeable. This could be an strategy of safeness and economy, once to change this parameter could increase the energetic expenditure and be more difficult to deal with any other miscalculation, even more for PD people. Change APAs appears to be a Moreover, PD people also were slower on step-2, indicating a massive difficult of trailing limb to deal with the obstacle. This could be explained by two mechanisms: 1) the bradykinesia due to loss of dopamine[27,28] and 2) the difficult imposed by avoid the obstacle without visual contact, demanding a higher control and a safe strategy which resulted in a slower movement for this step.

4.2) Higher vs lower obstacle: challenging vs visual cue?

Higher obstacles are more challenging than lower obstacles during gait initiation. To avoid a high obstacle during gait initiation coincided with more AP-displacement of the CoP. Increasing momentum for safe crossing[29] and toe-clearance – the participants have to increase the limb height for higher obstacle – explain the greater displacement in AP direction. Moreover, both groups also adopted a larger base of support (step width) for higher obstacles and participants with PD also increased step width for the intermediate obstacle and horizontal obstacle-foot distance of the leading limb for the high obstacle. These spatial adaptations deal with the instability caused by obstacle avoidance. This reduced ability is strictly related to PD group, considering to this group has a poorer capacity to activate muscle fibers[1], which increases the risk of touching the obstacle. The reduction (no) visual contact with the obstacle when the trailing limb avoids the obstacle challenges more movement control[3,30], resulting in a closer vertical distance to the obstacle in the PD group and increasing obstacle contact risky. Thus, gait initiation with an obstacle is a dangerous task for PD patients, once they need more time to adjust themselves if any disturbance occurs.

Obstacles might act as a visual cue for people with PD. It is possible that people with PD used it as a trigger, generating a great amount of information for motor output, resulting in a better motor programming[10,30] and offsetting the mechanical challenge imposed by the obstacle, causing limited effects of PD on crossing of low and intermediate obstacles. For small obstacles, no changes were found maybe because the presence of the obstacle works as a sensory cue[13,15]. Visual cues can help people with PD during gait and freezing episodes[13,30]. It improves motor signal output, resulting in a better gait performance. This finding is contrary to ongoing gait where low obstacles are linked to greater risk of falls and high variability in the last step before crossing[4]. Moreover, small obstacle could be a cue related to toe-clearance, indicating that the patient with PD should raise their foot in order to avoid then[13], which is not

difficult task considering the low obstacle height, improving gait initiation. However, this did not happen when the task became more challenging (high obstacle), requiring other adjustments to perform the task - both groups changed APAs parameters.

Limitations and conclusions

This study has some limitations that need consideration. The literature is very consistent in indicating lower muscle activation of people with PD during gait initiation[1], but we did not measure electromyography, maybe it would be an option for future studies. Future studies are needed to delineate the obstacle height that unimpaired gait initiation in PD patients. Finally, we did not measure if participants look or not at the obstacle during gait initiation. So, our explanation that the obstacle was used as a visual cue needs to be considered carefully, and tested in future studies.

In conclusion, obstacle presence and obstacle height influenced gait initiation in people with PD. Up to 15 cm, people with PD may deal with obstacle presence without any adjustment of APAs. However, for higher obstacles, an interaction of group and obstacle height suggested that crossing higher obstacle during the first step is more challenging for PD patients than neurologically healthy controls. For smaller obstacles the beneficial effect of a probable visual cue provided by the obstacle may help them with the challenge imposed by obstacle crossing for people with PD.

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Tables

Table 1. Means and standard deviations for clinical and demographic parameters of both PD group and control group. MMSE: Mini-Mental Status Exam; UPDRS: Unified Parkinson's Disease Rating Scale; H&Y: Hoehn & Yahr Scale

	PD group (8 males)	control group (9 males)
Age(years)	68±7	67±6
Body mass (kg)	69.1±17.4	76.7±15.4
Height (m)	1.60±0.10	1.60±0.08
MMSE (points)	27.2±3.1	26.9±2.2
UPDRS (points)	32.4±8.4	-----
H&Y (points)	2.1±0.2 (from 1-2.5)	-----

Table 2. Means and standard deviations of all spatial-temporal parameters analyzed in three condition for obstacle height comparison. § - condition effect compared to intermediate obstacle; *group*condition interaction.

	PD group		Control group	
	Step-1	**Step-2**	**Step-1**	**Step-2**
Low obstacle				
Stride length (cm)[#]	51.62±7.6	48.89±8.3	58.45±6.3	54.81±7.6
Stride width (cm)	13.84±5.6	6.01±2.6	12.79±5.2	6.44±2.2
Stride duration (s)	0.85±0.1	0.88±0.1	0.70±0.1	0.54±0.3
Stride velocity (cm/s)	62.32±9.7	60.47±12.6	81.64±11.2	77.13±13.8
Double support time (s)	0.37±0.1	0.44±0.1	0.50±0.2	0.37±0.1
Intermediate obstacle				
Stride length (cm)	56.44±5.0	49.82±6.1	60.22±4.8	53.92±10.3
Stride width (cm)	18.25±4.9*	10.71±4.8	13.91±5.2*	5.72±2.3
Stride duration (s)	0.98±0.1	0.94±0.1	0.80±0.1	0.76±0.1
Stride velocity (cm/s)	60.20±8.2	52.05±7.9	75.91±12.1	67.08±15.9
Double support time (s)	0.41±0.2	0.42±0.1	0.40±0.1	0.33±0.1
High obstacle				
Stride length (cm)	55.29±5.7	46.90±6.8[§]	58.78±6.1[§]	53.75±9.4
Stride width (cm)	17.59±3.2*	15.12±1.2	15.54±4.9*	5.28±3.3
Stride duration (s)	1.02±0.1	0.92±0.7	0.87±0.1	0.68±0.1
Stride velocity (cm/s)	56.42±10.6	48.00±10.2	69.43±13.3	62.43±15.6
Double support time (s)	0.53±0.1	0.41±0.1	0.36±0.1	0.30±0.1

Figures

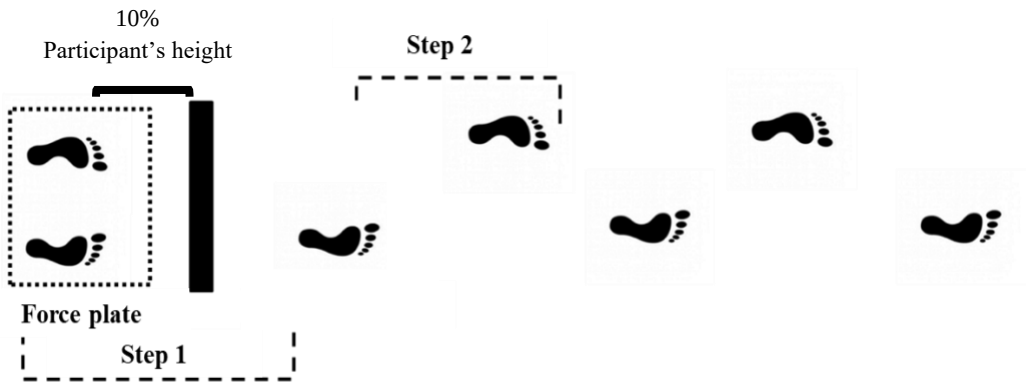


Figure 1. Schematic of data collection with obstacle avoidance. The dotted rectangle is the force plate. The black filled rectangle represents the obstacle. The distance between obstacle and start position was 10% of subject's height.

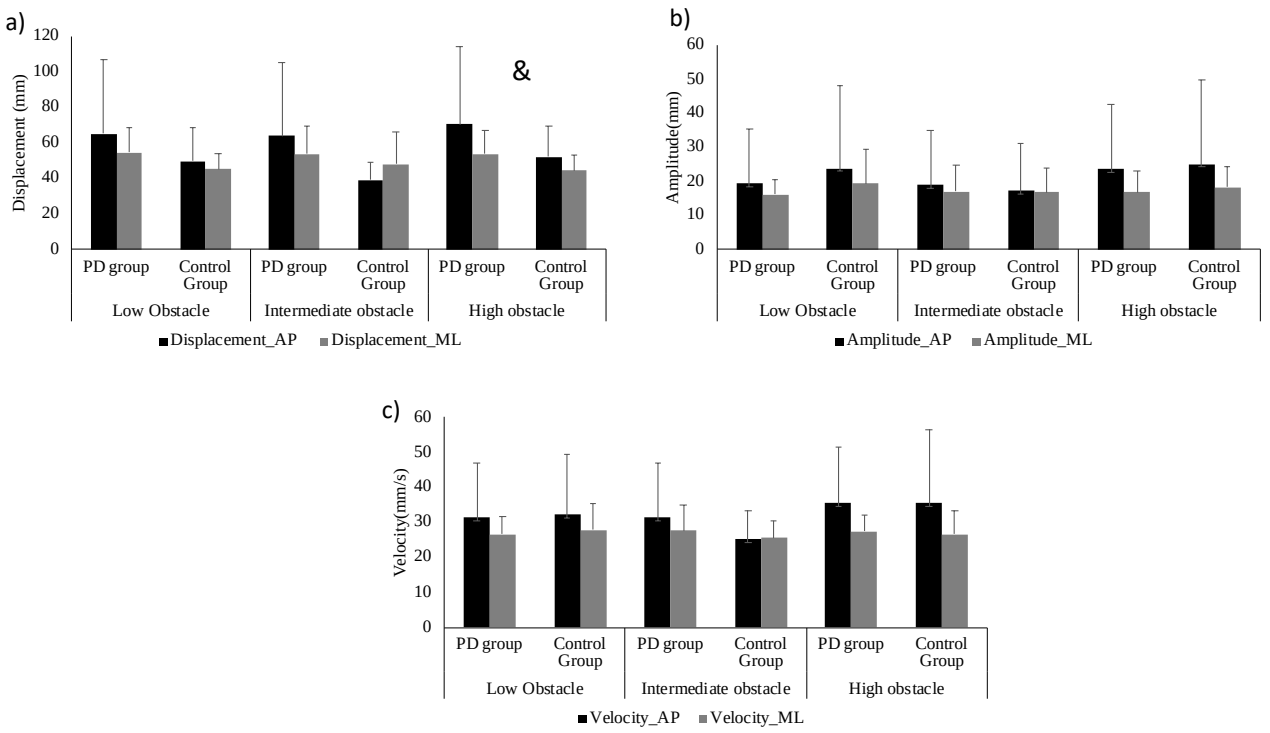


Figure 2. APA parameters for both groups and all conditions analyzed. &: high obstacle difference between intermediate for AP-displacement.

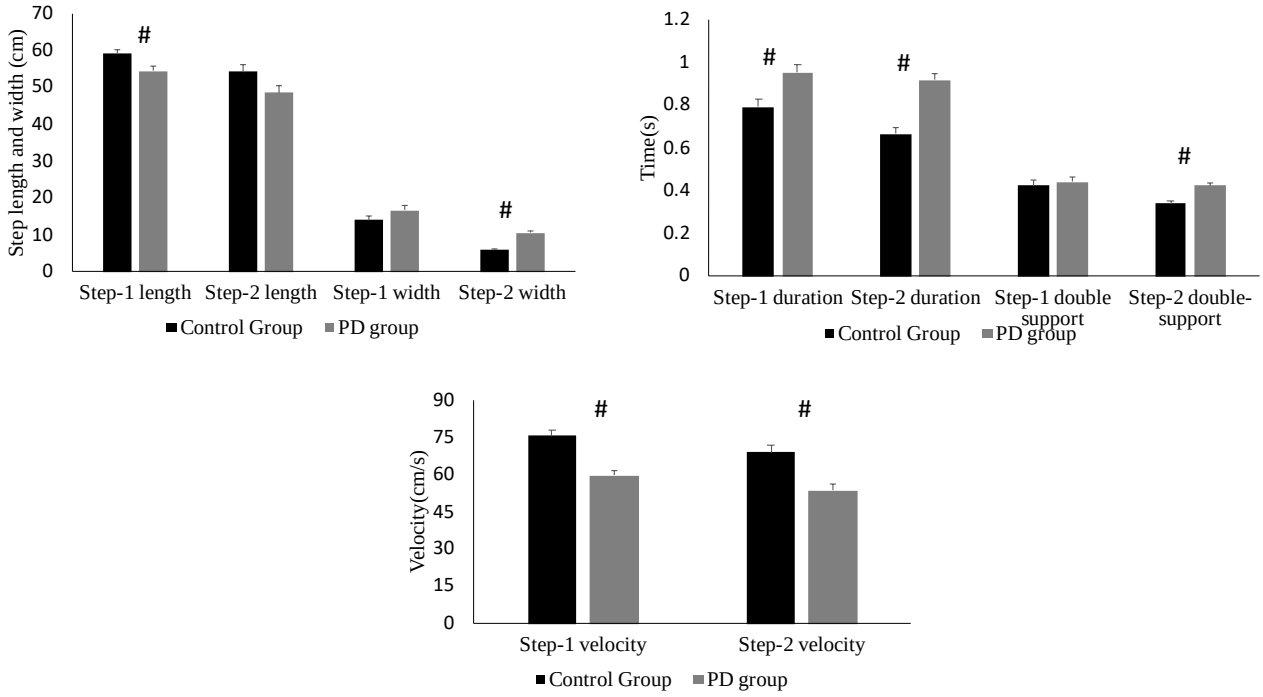


Figure 3. Gait initiation with obstacle parameters for step-1 and step-2. #: indicate a group difference

Study 3 - Effect of cognitive load on gait initiation: changes only on spatial-temporal parameters, but APAs are not changed.

Introduction

Besides characterized motor signals, PD people show impaired executive function compared to neurological health older people (DIRNBERGER; JAHANSHAHI, 2013). Executive functions could be defined as all process related to an action, since its goal formulation until the corrected execution and its results, after the action has been done (DIRNBERGER; JAHANSHAHI, 2013). In PD people, the neurodegeneration of dopaminergic neurons in substantia nigra advances to nucleus caudate and striatum, limbic nucleus and neocortical regions, affecting complex motor tasks (ROCHESTER et al., 2009). Thus, people with PD need to rely more on cortical areas to perform automatic movements (REDGRAVE et al., 2010). This behavior mostly happens due to putamen posterior degeneration once it is responsible for voluntary movements control and turns the movement more dependent of more intact areas (preserved), such as rostral-medial striatum. This "alternation" of voluntary control (basal ganglia to cortex) reflects the worsening during tasks which demands cognitive process (like dual-task situation).

In healthy older people, the performance of simultaneous tasks occurs in parallel, with a little influence on automatic task (REDGRAVES et al., 2010). However, PD people perform parallel processing when performing a complex task (such as obstacle avoidance with a simultaneous cognitive task), needing an extra processing compared to healthy older people, which make them slower in movement execution and with a worse performance (DIRNBERGER et al., 2005). During gait initiation under dual-task effect, PD people increase the number of errors in a cognitive task, prioritize the gait, once there is no effect on APAs in this condition (NOCERA; ROEMMICH; ELROD; ALTMANN; HASS; et al., 2013). Nevertheless, the literature lacks data about gait initiation with a challenging task (dual-task).

This study aims to investigate the effect of cognitive load (dual-task performance) during gait initiation with and without obstacle avoidance in PD people and their healthy matched-control (control group). We expect that during gait initiation with a cognitive task and obstacle avoidance, due to this cognitive overload, PD people decrease the number of APAs and spatial-temporal parameters (horizontal and vertical distance to the obstacle) compared to control group.

Materials and method

Thirteen PD people and 13 healthy matched-control participated in this study, according to statistical test on "G-power." The number of participants was based on a power analysis using an alfa level of 0.05 and a power of 95% and data on APAs from Delval and colleagues(DELVAL, ARNAUD et al., 2014) (G-power) – the analysis indicated a minimum number of eleven people in each group. To participate, PD patient had the disease diagnosis by a neurologist according to London Brain Bank (HUGHES et al., 1992). PD group and control group have been paired by anthropometric parameters. Clinical evaluation was composed by UPDRS and Hoehn & Yahr scale for PD group and MMSE (ALMEIDA, 1998), inclusion and exclusion criteria had been the same of other studies presented.

Before starting the trial, the participant was asked to close the eyes to avoid a priori planning according to the condition. Only after the command to start the trial ("Go"), the participant opened the eyes and performed the task. The evaluator reinforced the importance to keep the eyes closed until after the "Go" command. If the participant did open the eyes, the trial was excluded and performed again. For obstacle avoidance conditions (Figure 1), the obstacle was positioned at 10% of the participant's height in front of the starting position. We've chosen to standard the distance of 10% of participant's height to prevent more difficult from those shorter, and it would be needed an "artificial" adaptation if we didn't. Participants were instructed to avoid contact with the obstacle. In this study, the participant performed 20

trials: 5 trials without obstacle avoidance, 5 trials with obstacle avoidance, 5 trials without obstacle avoidance with a cognitive task and 5 trials with obstacle avoidance and a cognitive task. Obstacle height was according to the previous study (the height that affects more gait initiation – high obstacle – 25 cm). All conditions and trials were randomized.

The dual task condition consisted in listening to an audio track with a random sequence of numbers (0 to 9), that will be the cognitive task. The participants will be instructed to quantify how many times a chosen number selected by the evaluator will appear during the audio track. For example, the participant was asked to count (without using their fingers or loud voice) how many times the number 2 was said in the sequence that was presented during the motor task, for example, 0,2,2,4,1,1,5,6,7,7,2,1,9,8,2. After the ending of the audio track, we asked the participant how many times he/she listened to the chosen number. We registered the number that the participant said and if it is correct or not (for example, 4 times, is a right answer/ 2 times – is a wrong answer). The following instruction was given to the participant: "You will hear a sequence of number. I just want you to quantify how many times the number X will appear on the audio track. When you finish the task, I will ask you about how many times it was said, right?" Before data collection, some training trial with the audio track was performed to make sure that the participant understood it. Moreover, the audio track started 5s before the command "Go." During this period, the participant kept with their eyes closed. The trials that the participant opens their eyes before this time were excluded and performed again.

Cognitive "cost"

To evaluate the cognitive demand ("cost" that cognitive task represents for the participant), we had used a Mental Effort Scale (OTTO et al., 2014). This scale is used to verify how the participant perceives their cognitive effort during the task, and it could indicate how much the dual task influences on the motor task. After the trial, the participants were asked about it, demonstrating in a scaled ruler how much they dedicated cognitive effort to perform

it: 0mm (no mental effort) up to 150mm (the greatest possible mental effort). They had to do a point or a line at this ruler to indicate mental effort (OTTO et al., 2014).

Statistical analysis

All data was analyzed on SPSS 23.0 for Windows® with 0.05 significance level. The Shapiro-Wilk and Levene's tests were used to verify the normal data distribution and variance homogeneity, respectively. We compared the participant characteristics and cognitive function between groups using the ANOVA one way. For spatial-temporal parameters, APAs and mental "cost" of gait initiation, we performed MANOVAs with factor for the groups (PD people x Control group), obstacle (gait initiation without obstacle x gait initiation with low obstacle avoidance x gait initiation with intermediate obstacle avoidance x gait initiation with high obstacle avoidance) and dual task (gait initiation without dual task x gait initiation without dual task). Tukey univariate tests were used performed to identify differences when the MANOVA revealed significant interactions.

Results

For participant characteristics, ANOVA did not reveal significant differences between groups in any of the parameters analyzed (Table 1). For obstacle conditions, we've registered 8 obstacle's touches for PD group (3 participants) and 3 obstacle's touches for control group (2 participants). Only for task difficult, the ANOVA indicated a more difficult perception of the task for PD group ($p<0.001$) compared to control group. All trials with obstacle touches were performed again and discarded from analysis.

Table 1. Means and standard deviations for clinical and demographic parameters of both PD group and control group. MMSE: Mini-Mental Status Exam; UPDRS: Unified Parkinson's Disease Rating Scale; H&Y: Hoehn & Yahr Scale

	PD group (8 males)	**control group (9 males)**
Age(years)	69±2	68±1
Body mass (kg)	67.2±9.4	67.7±5.4
Height (m)	1.63±0.05	1.68±0.06
MMSE (points)	28.2±2.1	29.1±2.2
UPDRS (points)	30.4±10.4	-----
H&Y (points)	2.1±0.2 (from 1-2.5)	-----
Task difficult(cm)*	10.97±2.6	7.5±1.5

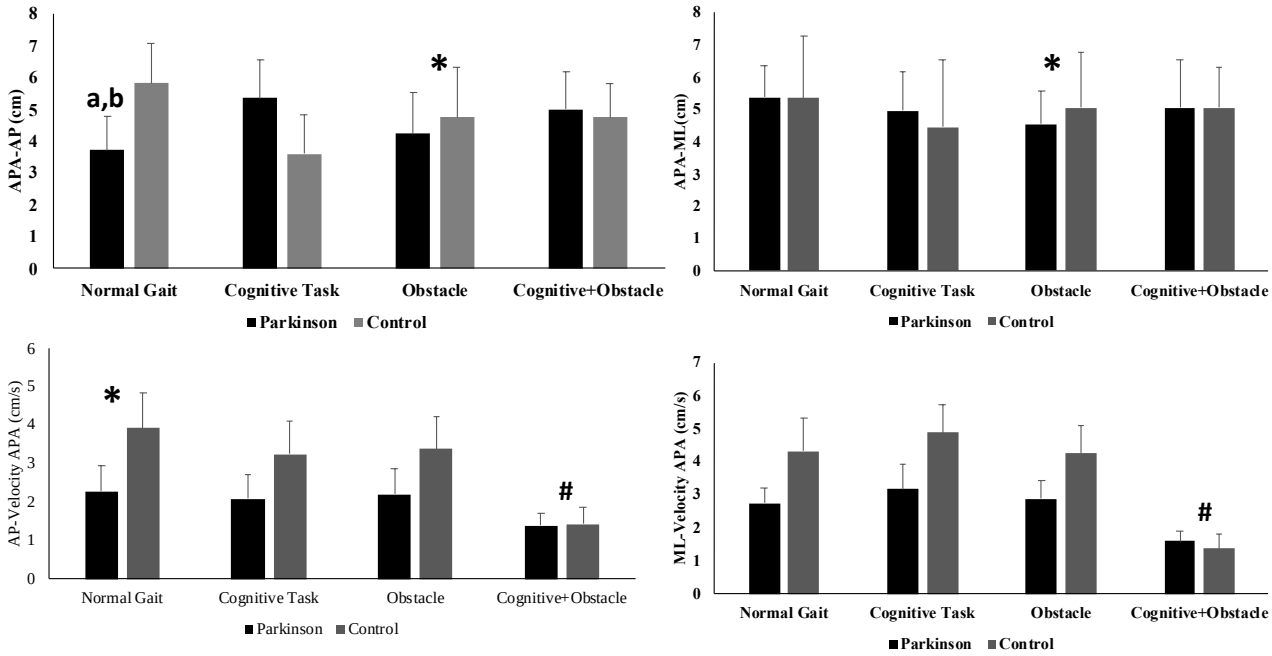
*group difference ($p<0.05$)

APAs parameters

There was a group difference only for APA velocity, for anteroposterior ($F_{1,24}$ = 63.126, $p<0.001$) and medio-lateral ($F_{1,24}$ = 79.553, $p<0.001$) direction. PD had slower movement of APA than Control Group for both APAs directions. For task effect, the MANOVA indicated a main effect for anteroposterior ($F_{3,72}$ = 29.132, $p<0.001$) and medio-lateral ($F_{3,72}$ = 64,474, $p<0.001$) velocity. The post hoc test indicated a slower APA velocity in both directions for the task with obstacle and cognitive task compared to all others conditions ($p<0.001$). The MANOVA also revealed a group*task interaction for anteroposterior APA displacement ($F_{3,72}$ = 12.026, $p<0.001$) and velocity ($F_{3,72}$ = 6.119, $p<0.001$) . The post hoc indicated, only for PD group, a smaller AP-APA displacement on normal gait (without obstacle

and cognitive task) compared to cognitive task only (p<0.002) and obstacle plus cognitive task (p<0.002).

Figure 2. APAs displacement and velocity during normal task, cognitive task and obstacle plus cognitive task. AP: anteroposterior; ML: medio-lateral. *: group difference (p<0.005)



*: group difference (p<0.005); #: task difference; a: normal gait is different from cognitive task; b: normal gait is different from cognitive+obstacle.

Spatial-temporal

The MANOVA indicated a main effect for group for step-1. PD group had presented smaller step length (p>0.007) and step velocity (p>0.001) and greater step width (p<0.001) and step duration (p<0.001) than control group. For step-2, there was the same behavior for group effect in all parameters analyzed.

The MANOVA also indicated a main effect for task. Only during gait initiation with obstacle avoidance with or without the cognitive task compared to gait initiation during normal gait and gait initiation plus cognitive task, both groups had a greater step-1 length (p<0.001). They also had a greater step width for gait initiation with cognitive task compared to gait

initiation without obstacle and without cognitive task ($p<0.03$). For step-2, the MANOVA indicated a main effect for group. The post-hoc indicated that PD had smaller values of step length, step velocity and greater values of step width and step duration compared to control group ($p<0.001$). There was also a main effect for task. During the condition with obstacle plus cognitive task, the step length was smaller ($p<0.003$) and the step width was wider ($p<0.002$) compared to normal gait. There were also a group*task interaction. The post hoc indicated that, in all tasks performed, step-2 length and velocity was greater for control group compared to PD group ($p<0.001$). On the other hand, for step-2 width, PD group shower greater step width compared to control group in all tasks performed.

Table 1. Mean±Standard deviations for spatial-temporal parameters in all conditions analyzed.

	Parkinson				Controle			
	Normal gait	**Cognitive**	**Obstacle**	**Cognitive+Obstacle**	**Normal gait**	**Cognitive**	**Obstacle**	**Cognitive+Obstacle**
Step-1 length*	51.58±4.5	48.17±3.9	54.25±3.2[c]	53.23±4.8[c]	53.88±4.6	52.03±3.3	55.44±2.4	54.07±2.3
Step-1 width	10.84±0.89	9.79±0.99	9.18±1.18	10.25±2.15	9.44±1.4	8.79±1.1	8.63±1.35	8.74±1.4
Step 1 duration	0.69±.06	0.70±.06	0.62±.05	0.70±.08	0.50±.04	0.54±.11	0.53±.07	0.53±.07
Step-1 velocity*	74.45±10.2	68.72±7.1	88.09±11.4	75.46±7.9	107.71±13.9	98.38±21.1	88.09±11.4	103.34±11.7
Step-2 length*	47.26±2.39	46.20±2.99	45.65±2.11	42.09±5.43	56.63±4.2	59.77±3.4	57.01±5.2	58.03±6.8
Step-2 width*	10.60±1.2	10.33±0.83	12.29±0.9	11.45±2.3	9.75±0.8	9.56±0.5	9.92±0.9	11.12±2.1
Step-2 duration	0.60±.05	0.62±.09	0.63±.08	0.65±.04	0.54±.02	0.54±.02	0.53±.03	0.55±.04
Step-2 velocity*	78.68±8.2	75.22±11.6	74.83±10.1	73.58±10.8	105.81±7.7	101.09±7.3	97.78±6.84	98.77±5.84

*: group difference ($p<0.05$), c: obstacle conditions with or without cognitive task are different from others conditions

Discussion

The study aims to investigate the effect of cognitive load (dual-task performance) during gait initiation with and without obstacle avoidance in PD people and their healthy matched-control (control group). We expect that during gait initiation with a cognitive task and obstacle avoidance, due to this cognitive overload, PD people decrease the number of APAs and spatial-temporal parameters (horizontal and vertical distance to the obstacle) compared to control group. Our results revealed some interesting points about gait initiation in complex environments: APAs changes are related to task difficult. Moreover, most of the changes were done on spatial-temporal parameters. On the following paragraphs, we will suggest some explanations for those findings.

APAs changes are related to task difficult. Despite the necessity that we need to adjust ourselves before an action, it is important to notice that APAs behavior was similar during gait initiation with or without obstacle or cognitive task. During the task with the combination of obstacle and cognitive task, both groups reduce APAs velocity to deal with the complex situation. Even in PD people, in which the dopaminergic system is compromised and the motor adjustments are impaired (TAKAKUSAKI et al., 2008; SIMIELI et al., 2015), APAs were not changeable during most of the tasks. This could be a strategy of safeness and economy, once to change this parameter could increase the energetic expenditure and be more difficult to deal with any other miscalculation (CARPENTER et al., 2006), even more for PD people.

Cognitive task maybe not interfere on gait initiation. Gait initiation is a complex moment of gait (DELVAL et al, 2014). Even under cognitive task effect, people with PD could perform a “safe” gait initiation, keeping APA and adapt mostly the second step. This strategy was a surprise for us, once most of other studies with gait initiation showed a great impair for people with PD (NOCERA; ROEMMICH; ELROD; ALTMANN; HASS, 2013; DELVAL, ARNAUD et al., 2014). The second step is not usually used in this previous study, but it is essential for more complex task, such those analyzed in this study. The second step deals with any disturbance, such as unbalances, that could occur during the first one (DIEËN, VAN et al., 2008; HAWKES et al., 2012). It’s possible that PD group chose to start with a safe strategy (based on gait initiation without

obstacle/cognitive task), and only change it if something happens (the combination of obstacle and cognitive task, for example). It´s not a very safe strategy though, once PD people are not able to deal with fast changes in body or environment (SIMIELI et al., 2018).

Despite the relevant findings, this study has some limitations that need further consideration. We did not measure if participants look or not at the obstacle during gait initiation. So, our explanation that the obstacle was used as a visual cue needs to be considered carefully and tested in future studies. Moreover, using some techniques that involve brain activity will be a great point to verify how PD people deal with overload situations during gait initiation.

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Study 4 – Sensory contributions during gait initiation – which information is more important for gait initiation?

Introduction

Sensory and perceptive deficits were recently identified in people with Parkinson's disease (PD) and might be a major role for movement disorders in this population. The basal ganglia involvement in sensory integration was recently determined (ALMEIDA et al., 2007; VITÓRIO et al., 2012) but there is a significant lack in how non-motor aspects, like sensory integration, could present an impact on gait initiation. When we walk straight toward an object, the vision is necessary to identify and judge the correct distance to that object, for example, an obstacle. Meanwhile, at the same time, the proprioception (sensory feedback by lower limbs muscle) provides information at each step as we move forward (PATLA, 2003).

Although, PD people are more dependent on visual feedback to plan and control their movement (VITÓRIO et al., 2012, 2013; PIERUCCINI-FARIA et al., 2013; SIMIELI et al., 2017; PEREIRA et al., 2019). Consequently, they have impairments on proprioceptive vias (ALMEIDA et al., 2007; TAKAKUSAKI et al., 2008) which impairs gait in complex environments. However, no previous studies analyzed the effect of sensory integration on gait initiation in PD people.

Based on that fact, this study aims to verify how the visual and proprioceptive information contributes to gait initiation with obstacle avoidance in people with PD and healthy-matched control in which we manipulated sensory information (visual and proprioception). We expect, in conditions that sensory information is manipulated, PD people increase the number and magnitude of APAs and spatial-temporal adjustments to perform the first step and they will need a greater number of gaze fixations to better planning gait initiation compared to the control group. We expect, yet, that proprioceptive manipulation impairs more sensory integration than visual manipulation, impairing gait initiation, mainly in PD people.

5.2. Materials and methods

Thirteen PD people and 13 healthy matched-control participated in this study, according to statistical test on "G-power." All PD people included in this study, had their disease diagnosis by a neurologist according

to London Brain Bank (HUGHES et al., 1992). PD group and control group were paired by age, gender, body mass and height. People with PD were assessed by UPDRS (Unified Parkinson's Disease Rating Scale (MDS et al., 2003) and classified by Hoehn & Yahr scale (HOEHN; YAHR, 1967). Both groups had their cognitive assessment made by MMSS (Mini-Mental Status Exam - (ALMEIDA, 1998)). The exclusion criteria

Spatial-temporal gait parameters were collected by a Vicon Motion System® with 8 cameras (Bonita System Cameras) sampling at a frequency of 200 Hz. For calculating these parameters, we used 39 reflected markers that were positioned according to the Full Body Plug-in-gait protocol (Vicon Motion System®). We calculated the length, width, duration, double support time (percentage of step duration) and velocity of the two first steps (Simieli et al, 2021). For APAs, a force plate (Accugait Force plate AMTI®) sampling at 200 Hz was positioned in the start position. APAs were determined as any adjustments/alteration in center of pressure (CoP) that occurred before apparent foot movement, based on displacement and velocity of the heel marker. APAs started with the initial movement of the CoP and ended when the CoP was in the most posterior and lateral in direction towards the stance leg. Anterior-posterior (AP) and medial-lateral (ML) displacement, amplitude and mean velocity were calculated for CoP position during gait initiation.

. For visual behavior, we used a system of Applied Sciences Laboratories® (ASL, Eye Tracking Mobile System – model Mobile Eye-XG). This device is monocular and was calibrated before and during trials. The data acquisition frequency was at 60Hz. After calibration, the participants performed few trials to familiarization with data collection environment. Gaze fixation was considered to inform the moments that visual information is acquired. Gaze fixation (duration >99ms) in gait initiation was analyzed by the number of fixations e mean duration of fixation (mean time of fixation) and fixation on the feet (the areas of interest, in this case, was only the feet (BARBIERI et al., 2016).

In this study, the participant performed 20 trials: 5 trials of gait initiation without sensory manipulation, 5 trials of gait initiation with visual manipulation (RIV), 5 trial of gait initiation of somatosensory manipulation (PSS) and 5 trials of gait initiation with somatosensory and visual manipulation (RISS). The obstacle was presented during all tasks. For obstacle avoidance conditions, the obstacle was positioned at 10% of the participant's height in front of the starting position. We've chosen to standard the

distance of 10% of participant's height in order to prevent more difficult from those shorter, and it would be needed an "artificial" adaptation if we didn't. Participants were instructed to avoid contact with the obstacle.

During RIV condition, we fixed a siding on participant's chest, so that he/she had no visual information about the lower limb. The siding was made by paperboard (black), without any overweight to the participant. For PSS manipulation, the participant started on foam with moderate density positioned on the force plate and they must stayed on this foam for gait initiation task. For RISS trial, both manipulations were present. To avoid falls, a team member was close to the participant.

Statistical analysis

Data was analyzed on SPSS 23.0 for Windows® with 0.05 significance level. The Shapiro-Wilk and Levene's tests were used to verify the normal data distribution and variance homogeneity, respectively. Participant characteristics and cognitive function were compared between groups using the ANOVA one-way for independent samples. For spatial-temporal parameters, APAs, and gaze behavior of gait initiation, we performed MANOVAs with a factor for groups (PD people x Control group) and sensory restriction (no restriction x RIV x PSS x RISS) with a repeated measure for the last factor. Tukey univariate tests was performed to identify differences when the MANOVA revealed significant interactions ($p<0.05$).

Results

For participant characteristics, ANOVA did not reveal significant differences between groups in any of the parameters analyzed (Table 1). For obstacle conditions, we've registered 12 obstacle's touches for PD group (4 participants) and 2 obstacle's touches for control group (2 participants). All trials with obstacle touches were performed again and discarded from analysis.

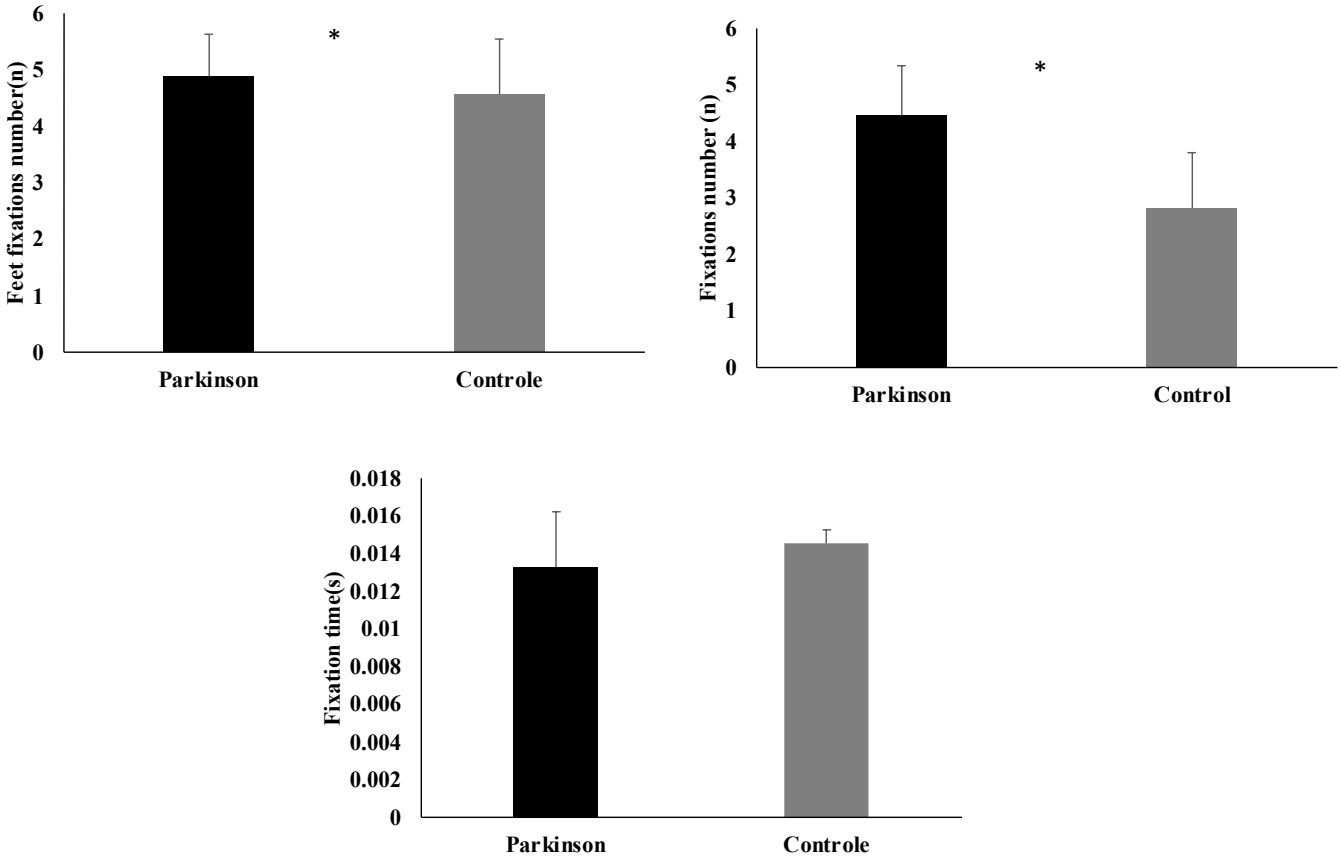
Table 1. Means and standard deviations for clinical and demographic parameters of both PD group and control group. MMSE: Mini-Mental Status Exam; UPDRS: Unified Parkinson's Disease Rating Scale; H&Y: Hoehn & Yahr Scale

	PD group (8 males)	**control group (9 males)**
Age(years)	69±2	68±1
Body mass (kg)	67.2±9.4	67.7±5.4
Height (m)	1.63±0.05	1.68±0.06
MMSE (points)	28.2±2.1	29.1±2.2
UPDRS (points)	30.4±10.4	-----
H&Y (points)	2.1±0.2 (from 1-2.5)	-----

Gaze parameters

The ANOVA indicated a main effect for group for gaze behavior parameters. The post hoc test revealed that PD group had a greater number of fixations ($p<0.001$) and more feet fixations ($p<0.001$) than control group. During RIV both groups increased fixation time compared to normal gait initiation ($p>0.001$). Moreover, during RIV, PD group needed more fixations on feet to perform gait initiation compared to control group ($p>0.001$).

Figure 2. Gaze parameters during RIV (visual restriction condition) for both groups analyzed. *: group difference



APA parameters

The MANOVA revealed a main effect for group for APAs parameters. The post hoc test indicated that for COP-displacement on AP-direction ($p<0.001$) direction, the PD group had smaller movement during APA than Control Group. Moreover, the MANOVA did not indicated significant main effect for task ($p>0.05$) or group*task interaction for APA ($p>0.05$).

Table 2. Step 1 (S-1) and Step 2 (S-2) means and standard values in all conditions performed. RIV: visual restriction; PSS: sensory perturbation (foam); RIVV: visual restriction + sensory perturbation. * group difference ($p<0.05$)

	Parkinson				**Control**			
	No restriction	**RIV**	**PSS**	**RISS**	**No restriction**	**RIV**	**PSS**	**RISS**
S-1 length	48.45±3.6*	53.64±3.1*	49.05±2.6*	51.99±4.8*	55.53±2.9*	57.63±4.1*	54.33±3.1*	56.58±7.6*
S-1 width	12.48±1.9	12.79±1.5	13.77±2.9	13.42±2.6	10.43±1.9	11.56±1.5	13.07±2.6	12.01±3.6
S-1 duration	0.59±.04	0.70±.06	0.71±.06	0.72±.09	0.56±.08	0.61±.11	0.62±.09	0.66±.08
S-1 velocity	81.74±10.56*	76.29±7.8*	68.82±8.9*	67.07±9.6*	99.74±17.1*	96.79±17.3*	89.02±14.1*	88.34±15.3*
S-2 length	50.09±3.0*	50.26±3.2*	50.53±3.2*	53.77±5.3*	56.63±4.2*	59.77±3.4*	57.01±5.2*	58.03±6.8*
S-2 width	11.75±1.9	11.60±2.27	11.23±1.86	10.75±1.76	10.11±1.9	10.78±1.3	10.27±1.5	10.01±2.3
S-2 duration	0.60±.04	0.62±.08	0.64±.09	0.67±.04	0.60±.06	0.54±.07	0.52±.08	0.58±.04
S-2 velocity	83.59±7.2*	81.31±11.0*	79.83±13.1*	78.83±12.3*	95.38±12.8*	110.65±15.5*	109.91±17.0*	100.07±16.1*

Spatial-temporal parameters

For step-1 and step-2, MANOVA indicated a main effect for group. PD group had a smaller step length ($p>0.001$) and slower step velocity($p<0.001$) compared to control group. On the other side, PD group had greater values of step duration ($p<0.002$) and step width ($p<0.001$) compared to control group.

For task effect, for the step-1, during RIV($p>0.003$) and RISS ($p>0.001$), step length and width was greater than gait initiation normal gait initiaion and PSS. There was no task difference for step-2. Moreover, the ANOVA did not indicate any group*task difference ($p>0.05$).

Discussion

This study aims to verify how the visual and proprioceptive information contributes to gait initiation with and without obstacle avoidance in people with PD and healthy-matched control. We expect, in conditions that sensory information is manipulated, PD people increase the number and magnitude of APAs and spatial-temporal adjustments to perform the first step and need a greater number of fixations to a better planning of movement than the control group. We expect, yet, that proprioceptive manipulation impairs more sensory integration than visual manipulation, impairing gait initiation, mainly in PD people. Our results showed a very curious information, that we are looking in a series of studies with gait initiation and complex environment: APA are task dependent. PD group have a preference to deal with external perturbation changing gait parameters instead APAs. The changing in APA parameters occurred more often during high complex situation (visual restriction, in this case). Moreover, visual information seems to be more important for gait initiation (BARBIERI et al., 2016) with

obstacle than sensory information of the feet. On the next paragraphs we will discuss about those findings.

Basal ganglia damage may be associated with sensory and perceptual deficits (PERRY et al., 2001; ALMEIDA et al., 2007)as well as right hemisphere damage, which is responsible for visuospatial processing (PEREIRA et al., 2019). On the other hand, reduced step velocity and step length increases instability during walking (BRUIJN et al., 2013). To deal with an unstable gait, people with PD increased the basis of support (stride width) during gait initiation. Those results are adding more evidence that bradykinesia is the main impairment in PD people. So, to deal with bradykinesia and complex environment situation, people with PD adopt a more conservative strategy finding on ongoing gait as well during gait initiation (wider step width (MORRIS et al., 2009; SIMIELI et al., 2017, 2018). This strategy, apparently, is safe enough for gait initiation once they could perform the task with success and no falls.

The greater dependency on visual obstacle information may be explained due to working memory and/or executive function deficits caused by the disease. PD group present difficulty remembering locations (AZULAY et al., 2006) and require eye movements to visual targets to take advantage of direct sensory-to-motor mapping in structures like the superior colliculus (TAKAKUSAKI et al., 2008). Declines in executive cognitive functioning require prolonged gaze fixation time on visual information during challenging walking situations, in our case the RIV, to compensate longer information processing duration. Despite gait initiation is a short task, it's notable the role of vision during this situation. Once the participant was eyes-closed before the commando "Go", once they opened their eyes, they needed to ensure where obstacle and their body was before starting the task. Due to the impairment on dopaminergic pathway, PD group needed to look for more information and for the feet more times compared to control group.

Despite all those relevant finding, our study had some limitations. The eye-tracker had a limitation area of capture, so, if the participant only moved their eyes to look down, the retina disappeared during recording, and it was impossible to track their gaze behavior. The number of subject was smaller (despite the relevance of G-power test) and a bigger sample could have a solid result.

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Final chapter

The present findings contribute to the scientific advancement of the area of research in which it belongs and can help to understand a behavior which is very present in daily life of the elderly population: gait initiation. Thus, the application of the main results and directions for future studies are highlighted below. Also, the work of health professionals to alleviate some effects of Parkinson's disease during the initiation of walking can be important. According to our results, people with PD are more cautious during gait initiation, regarding changes during more complex situations, such as during dual-task situation or during higher obstacles situations. The next paragraphs will explore how those findings could be important for PD populations as well for health professionals.

This thesis evidenced the behavior of APAs during more complex situations, such as obstacle avoidance, dual-task situations, and sensorial restriction. The results highlighted the fact that APA are changeable during those complex situations, for both groups (Parkinson group and healthy elderly). Moreover, APAs behavior was in accordance with previous studies, once people with PD have impairments during APAs (slower and smaller compared to control Group). In this way, other strategies can be adopted to improve early preparation, for example, to avoid an obstacle. The changes start to become more evident in APAs as the environment became more complex, which can be harmful for people with Parkinson's disease. Even during “easier” situation, it is important to prepare themselves to start gait, or they will not have enough time to correct, once the pathology compromise other components of gait, such as, the reaction time. One example of greater environmet complexity occurred during gait initiation with obstacle avoidance and dual-task situation (backward counting). Despite the specific situation of this study, it is a regular situation which occurs daily, and PD people could not be prepare for this. Moreover, the task is an important issue to analyze APA, once the adaptations

of APAs are direct related to task complexity. Health professionals need to know about this information to develop the intervention with this type of special population.

The non-motor symptoms of Parkinson's disease, often overlooked during motor processes, need to be considered for gait analysis. By withdrawing or restricting sensory information such as vision, it possible to change gait behavior in people with PD more vulnerable and tend to adopt a conservative gait pattern and it could be a risky situation. Other previous studies finding a great dependence of people with PD to vision. This situation, with limited visual information is common during our day. Such as when we are talking with someone and deviate our gaze from ground to person's face (for example). If our work memory is good enough to deal with this situation, gait behavior will not change. However, for people with PD, it is important to highlight that the great dependence of visual information and the restriction to this, could be a very risky situation. Despite the success in the task, patterns considered risky in the literature, such as slower step speed, were often adopted. Thus, the importance of the gait initiation for the daily life of people with Parkinson's disease and neurologically healthy is evident. Strategies for safer gait initiation in PD people could be more explored, such as the use of visual cues (stripes on the floor, for example). This strategy is a an excellent to be used at home, avoiding falls situations and the change of falls complications, such as, hospitalization.

The last point of this chapter is related to future studies related to gait initiation. Once technology is evolving and the possibility of brain analyzes become less invasive, it is important to know what is happening inside the brain of people with PD during this task. If, in the future, the researchers finding the link of brain and gait initiation impairments, the treatment and the interventions will be better delineated. Despite it is known that some brain areas, such as, basal ganglia, pedunculus pontine nuclei and mesencephalic locomotor area are related to gait initiation, this information is more theory than practical. Other important point for future

studies will be understanding the drug effect during gait initiation. Only one study tried to investigate, and the findings were that L-dopa is not effective for gait initiation. However, according to other studies, it is important to create challenging situations to verify the effect of L-dopa. In this context, if people with PD without medication deals with a complex environment (obstacle plus dual task) and repeat again during "ON" state of medication, it is possible to verify some contributions of L-dopa more than compared to normal environment.

The conclusion of APAs and complex task of this thesis are APA behavior are dependent of task complexity, PD people present worse APA behavior compared to healthy people (slower and smaller - COP velocity and displacement), visual information is a crucial point for gait initiation in PD people. These three key points are important to fill the gap in the literature related to gait initiation and Parkinson's disease. Moreover, the above points for future studies will advance even more to understand this complex moment of gait, and it will be very helpful to understand why this situation have a great correlation with falls.

ANEXO 1 – PARECER DO COMITÊ DE ÉTICA EM PESQUISA LOCAL (ETHICAL COMITEE APPROVAL)

UNESP - FACULDADE DE CIÊNCIAS CAMPUS BAURU - JÚLIO DE MESQUITA FILHO

COMPROVANTE DE ENVIO DO PROJETO

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: INICIAÇÃO DO ANDAR E DOENÇA DE PARKINSON: INFLUÊNCIA DA PRESENÇA DE UM OBSTÁCULO, DA TAREFA COGNITIVA E DA INFORMAÇÃO SENSORIAL

Pesquisador: Lucas Simieli

Versão: 1

CAAE: 64921917.9.0000.5398

Instituição Proponente: UNIVERSIDADE ESTADUAL PAULISTA JULIO DE MESQUITA FILHO

DADOS DO COMPROVANTE

Número do Comprovante: 012682/2017

Patrocionador Principal: Financiamento Próprio

Informamos que o projeto INICIAÇÃO DO ANDAR E DOENÇA DE PARKINSON: INFLUÊNCIA DA PRESENÇA DE UM OBSTÁCULO, DA TAREFA COGNITIVA E DA INFORMAÇÃO SENSORIAL que tem como pesquisador responsável Lucas Simieli, foi recebido para análise ética no CEP UNESP - Faculdade de Ciências Campus Bauru - Júlio de Mesquita Filho em 17/02/2017 às 15:43.

Endereço: Av. Eng. Luiz Edmundo Carrijo Coube, nº 14-01
Bairro: CENTRO **CEP:** 17.033-360
UF: SP **Município:** BAURU
Telefone: (14)3103-9400 **Fax:** (14)3103-9400 **E-mail:** cepesquisa.fc@unesp.br

ANEXO 2 – TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (AGREEMENT FORM)

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

IB/UNESP/Rio Claro

(Conselho Nacional de Saúde, Resolução 466/12)

Eu, Prof. Me. Lucas Simieli, RG: 46530292-0; CPF: 384.125.468.30, convido Vossa Senhoria a participar de uma pesquisa referente à pesquisa Tese de Doutorado denominada "Iniciação do andar e doença de parkinson: influência da presença de um obstáculo, da tarefa cognitiva e da informação sensorial ", que tem como membro participantes da equipe de pesquisa oProf. Dr. Fabio Augusto Barbieri e os aluno de mestrado Luis Felipe Itikawa Imaizumi, André Macari Baptista, Tiago Penedo e Vinicius Alota Ignácio Pereira a realizar-se na Faculdade de Ciencias da UNESP/Bauru, no MOVI-LAB – Laboratório de Pesquisa em Movimento Humano, endereço: Av. Engenheiro Luiz Edmundo Carrijo Coube, 14-01,Vargem Limpa CEP: 17033-360, Fone: (14) 3103-6000, Fax: (14) 3103-6000. O objetivo do estudo é investigar o efeito da presença de obstáculo, da tarefa dupla e da restrição sensorial durante o início do andar em pacientes com DP. Nós sabemos que essa doença pode alterar os padrões da marcha e que devido aos comprometimentos acarretados pela doença, existe a maior chance de ocorrer quedas e uma maior dificuldade em iniciar o andar, tornando importante o entendimento dessa fase do andar em ambientes comuns do dia-a-dia, como a ultrapassagem de obstáculos. Para melhor entendermos esses mecanismos, Vossa Senhoria está sendo convidada a participar do seguinte plano de atividades:

1˚ dia - a) Anamnese completa sobre doenças, lesões, medicamentos em uso, tempo com DP, número de quedas, entre outras informações relevantes para verificar a ausência dos critérios de exclusão. Este procedimento será realizado juntamente com o cuidador do participante; Avaliação cognitiva e clínica do paciente (para idoso com DP), a ser realizada por avaliador experiente treinado por neuropsiquiatra membro da equipe, para caracterização da amostra e do grau de acometimento dos pacientes, através de uma bateria de exames específicos.

b) Realização da tarefa do andar com ultrapassagem de obstáculos, tarefa concomitante e restrição sensorial para aquisição das variáveis de interesse.

As duas etapas serão realizadas em um único dia, desta forma, Vossa Senhoria deverá comparecer em um único dia no MOVI-LAB – Laboratório de Pesquisa em Movimento Humano, localizado na Faculdade de Ciencias da UNESP/Bauru. Todas as tarefas serão registradas em um aparelho específico para análise do andar e, para isto, será necessário vestir uma calça de lycra com uma camiseta, para que possamos fixar alguns objetos (marcadores passivos) sobre a roupa. Além disso, uma vez que será analisado o comportamento muscular, será necessário realizar a tricotomia do local (perna – região da panturrilha e "canela"). Esse procedimento não é invasivo e não provoca dor. Também usará um óculos que nos permitiriá saber para onde o senhor(a) estará olhando. Todos os procedimento servirão para medir seu movimento com mais precisão. Sua participação não deverá exceder 60 minutos de duração.

Todos os procedimentos serão realizados pelo mesmo grupo de pessoas. Apesar de estas atividades possuírem um alto grau de segurança, é necessário ressaltar que há algum risco de queda ou de desconforto, mas nossa equipe estará sempre com você para qualquer problema. Os cuidadores dos idosos poderão permanecer dentro da sala durante a coleta de dados. Os resultados deste estudo poderão servir para auxiliar no deslocamento diário e entendimento da doença de Parkinson nos padrões do início do andar e como o obstáculo, tarefa dupla e restrição sensorial podem influenciá-la. Além de permitir que sejam criadas sessões de treinamentos que possam auxiliar nas possíveis dificuldades que serão encontradas, a fim de diminuir os desequilíbrios e, consequentemente, as quedas.

Vossa Senhoria poderá esclarecer qualquer dúvida a respeito do estudo e dos procedimentos acima descritos, pois teremos a obrigação de respondê-las a qualquer momento. Vossa Senhoria terá plena liberdade para recusar a participação no estudo ou abandoná-lo a qualquer momento sem qualquer penalidade. Além disso, não haverá remuneração, bem como gastos e/ou prejuízos financeiros.

Para um maior controle deste estudo, Vossa Senhoria receberá um código, o que assegurará que a sua identidade e dados coletados se mantenham confidenciais. Todos os resultados do estudo serão usados, única e exclusivamente, para fins de ensino e pesquisa e todas as informações pessoais serão mantidas em sigilo. Vossa Senhoria terá a liberdade de solicitar, a qualquer momento, informações sobre os resultados das tarefas realizadas.

Se Vossa senhoria se sentir suficientemente esclarecido sobre essa pesquisa, seus objetivos, eventuais riscos e benefícios, convido-o(a) a assinar este Termo, elaborado em duas vias, sendo que uma ficará com vossa senhoria e outra com o pesquisador.

_____, _____ de _____ de ____.

Assinatura do participante _____

Assinatura do pesquisador:

Prof. Me. Lucas Simieli _____

Telefone: (19) 9-9186-6294

Nome do participante: _____

Documento de Identidade no. _____Sexo: _____

Data de Nascimento: ____/____/____

Endereço: _____

Bairro:_____ Cidade: _____

CEP: _____ Fone: (_____) _____

Código do participante: _____